



Review Article

# Diagnosing Pneumonia in Real Time: Rapid Diagnostic Tests as Game-Changers in Management Strategies

Nurgul Ablakimova

Department of Pharmacology, West Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan

## Abstract

This review explores the transformative impact of rapid diagnostic tests (RDTs) on pneumonia management. Pneumonia, a global health challenge, often requires swift identification of causative pathogens for effective treatment. Traditional diagnostic methods, while valuable, have limitations, prompting the rise of RDTs. The review highlights the advantages, challenges, and future directions of RDTs, emphasizing their potential to provide real-time pathogen identification, improve treatment strategies, and enhance patient care in the context of pneumonia.

**Keywords:** pneumonia, pathogen, antibiotic resistance, global health, diagnostics

Corresponding Author: Nurgul Ablakimova; email: n.ablakimova@zkmj.kz

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## 1. Introduction

Pneumonia, a prevalent respiratory infection, remains a substantial global health challenge due to its potential severity and impact on public health [1]. In spite of the swift advancement in novel therapies, pneumonia remains a significant contributor to elevated rates of health complications and mortality [2]. Characterized as a sudden infection affecting the lung's parenchyma, it arises from a diverse range of microorganisms, encompassing bacteria, viruses, and fungi [3]. The identification of the responsible organism becomes exceptionally valuable when it leads to a shift in treatment approach. Diagnostic strategies exhibit variability based on the seriousness of the ailment and the suspected pathogen. The consensus among most healthcare practitioners is that microbiologic tests in outpatient

settings are likely to yield limited results and contribute minimally to the selection and duration of antibiotic courses [4]. Among hospitalized individuals, especially those afflicted by severe sepsis or septic shock, pinpointing the causative microorganism can notably enhance survival rates [5]. For all hospitalized patients who exhibit purulent sputum, it is imperative to subject it to Gram staining and culture analysis [6]. In scenarios where patients lack purulent sputum or are incapable of providing lower respiratory samples, culture outcomes may lack precision and frequently reflect upper respiratory tract or oropharyngeal colonizers rather than actual pathogens [7]. Routine blood cultures in cases of pneumonia exhibit minimal effectiveness and usefulness, regardless of the severity and risk factors involved [8]. Moreover, collecting cultures after the initiation



of antibiotic therapy can significantly impact diagnostic informativeness [9]. Early and accurate diagnosis is a cornerstone of effective pneumonia management [10]. The advent of rapid diagnostic tests (RDTs) has ushered in a new era of diagnostics, promising real-time identification of pathogens and influencing treatment strategies [11]. In this review, we explore the transformative potential of RDTs in the management of pneumonia.

## 2. Traditional Diagnostic Approaches for Pneumonia

The typical manifestation of pneumonia involves the sudden onset of infectious symptoms affecting the lower respiratory tract, accompanied by consistent radiographic patterns. These symptoms often encompass fever, cough, pleurisy, shortness of breath, and heightened sputum production. However, pneumonia's presentation can deviate from the norm, with some individuals primarily experiencing nonrespiratory symptoms like general discomfort, muscle pain, confusion, and diarrhea. Among the elderly, this atypical presentation may occur more frequently, potentially causing delays in treatment and elevated mortality rates. To establish a pneumonia diagnosis, it's crucial to have radiographic evidence of lung involvement. The appearance of pneumonia on radiographs can vary significantly. While computed tomography (CT) offers the most detailed detection of lung infiltrates, plain chest X-rays are more common, especially in outpatient settings. Although CT scans provide more specific information (refer to Figures 1D–F), they have downsides such as increased radiation exposure, inability to be done at the bedside, and real-time interpretation challenges.

Plain chest X-rays have a limited sensitivity of 38%–75% for identifying infiltrates. In critical cases, the less optimal anteroposterior view is often used,

and image quality suffers due to factors like weak inhalation, obesity, and suboptimal positioning.

Point-of-care ultrasonography has emerged as an alternative to plain chest X-rays for detecting lung consolidations. Its advantages include real-time bedside imaging and interpretation, absence of radiation exposure, and better sensitivity compared to X-rays. Distinguishing between lung consolidation and pleural effusion is also easier with ultrasonography. However, achieving sensitivities above 95%, as reported in some literature, requires skilled practitioners to evaluate the lungs from various angles, which can be time-consuming.

For individuals suspected of having pneumonia, standard laboratory tests are generally recommended, particularly when hospitalization becomes necessary. A complete blood cell count can reveal an elevated white blood cell count or the presence of immature white blood cells, indicative of an acute infection. Serum chemistry analysis can offer insights into potential organ involvement, like liver or kidney dysfunction, and contribute valuable data for assessing the severity of pneumonia.

Procalcitonin (PCT) is a serum protein that gets released when the body responds to bacterial infections. Notably, its release is suppressed during viral infections through the action of interferon gamma, an inhibitory cytokine. This characteristic renders PCT a valuable biomarker for distinguishing between viral and bacterial causes of community-acquired pneumonia (CAP). In various studies involving both outpatient and inpatient groups, setting a lower threshold value for PCT has been shown to discourage unnecessary antibiotic use, resulting in reduced antibiotic consumption without adversely affecting mortality rates. However, due to the significant risks associated with delaying or withholding essential antibiotics in pneumonia, there isn't a unanimous consensus on the routine use of PCT in this context. Moreover,

the latest treatment guidelines do not currently include its routine use.

Traditional methods of diagnosing pneumonia, including clinical assessment, chest radiography, and microbiological testing, have long been the mainstays of medical practice. While these methods have provided valuable insights into the presence of infection, they are not without limitations. Clinical symptoms often overlap with other respiratory conditions [12], chest radiography lacks specificity [12], and microbiological cultures can be time-consuming and result in false positives due to contamination [13].

### 3. The Rise of Rapid Diagnostic Tests

The emergence of RDTs represents a paradigm shift in pneumonia diagnostics. These tests harness advanced molecular and immunochromatographic technologies to swiftly detect specific pathogen markers (Table 1) [14]. The speed of these tests has the potential to transform the diagnostic landscape, enabling real-time identification and timely initiation of appropriate treatment [15]. Unlike traditional methods that rely on time-consuming cultures or complex molecular assays, RDTs deliver results within minutes, allowing healthcare providers to make prompt and precise treatment decisions. This advancement is particularly crucial in the context of pneumonia, where timely intervention can be a matter of life and death. Furthermore, RDTs are instrumental in combatting the global challenge of antibiotic resistance, as they enable clinicians to differentiate between bacterial and viral infections, reducing unnecessary antibiotic prescriptions [16]. As we witness the rise of RDTs in the field of pneumonia diagnosis, we move closer to achieving more efficient and targeted patient care, ultimately improving outcomes for individuals affected by this respiratory condition. Urinary antigen testing has gained widespread

popularity for numerous impactful respiratory infections, notably those caused by *Legionella pneumophila* (*L.pneumophila*) and *Streptococcus pneumoniae* (*S.pneumoniae*) [17]. These tests are considerably less affected by previous antibiotic treatment compared to sputum or blood culture [18].

### 4. Mechanisms and Technologies Behind Rapid Diagnostic Tests

**Antigen shedding:** When a person is infected with certain bacteria, such as *L.pneumophila* or *S.pneumoniae*, the bacteria shed specific antigens. Antigens are substances produced by the bacteria that trigger an immune response in the body.

**Urine collection:** The patient provides a urine sample. Unlike traditional diagnostic methods that require samples from the respiratory tract, urinary antigen tests offer a noninvasive and easily accessible alternative.

**Immunoassay detection:** The urine sample is then subjected to an immunoassay, which is a laboratory technique that relies on the specific binding of antibodies to antigens. In the case of urinary antigen testing, the test employs capture antibodies that are specific to the antigens produced by the target bacteria (Figure 1).

**Enzyme-Linked Immunosorbent Assay (ELISA) or Immunochromatographic/Lateral Flow Assay (LFA):** The immunoassay can take different forms, such as an enzyme-linked immunosorbent assay (ELISA) or an immunochromatographic/lateral flow assay (LFA). ELISA involves the use of enzymes to produce a color change when the target antigen is present. LFA, on the other hand, produces visible lines on a test strip [17].

**Positive or negative result:** If the specific antigens related to *L.pneumophila* or *S.pneumoniae* are present in the urine, the test will yield a positive result. This indicates an active infection with the

TABLE 1: Comparison of detection methods of pneumonia pathogens.

Test	Time	Advantages and Disadvantages
Culture method	3–7 days	Likely to identify true pathogen if detected. It is advisable to isolate it for susceptibility testing and conduct further investigations such as serotyping and sequencing. Obtaining a high-quality specimen from sputum can be challenging, and it's important to note that bacteremia is not always linked with pneumonia.
Molecular assays	2–4 hours	Rapid outcomes, high sensitivity, and the potential inclusion of susceptibility or other genetic markers (such as species or serotyping) are advantages. However, there is no isolate available for additional testing, and the approach lacks standardization, with various laboratory-developed tests in use.
Serology	2 hours–2 days	Valuable for epidemiological investigations and capable of differentiating <i>Pneumococcus</i> serotypes. However, not suitable for acute diagnosis, lacks an isolate for additional testing, and results may be influenced by prior pneumococcal vaccination.
Urinary antigen test	15 minutes	Swift and highly specific, enabling prompt adjustments to therapy upon a positive result, FDA-approved tests are accessible. Narrow number of pathogens that can be identified. Moreover, there is no isolate for subsequent testing.

respective pathogen. Conversely, a negative result suggests the absence of these specific antigens.

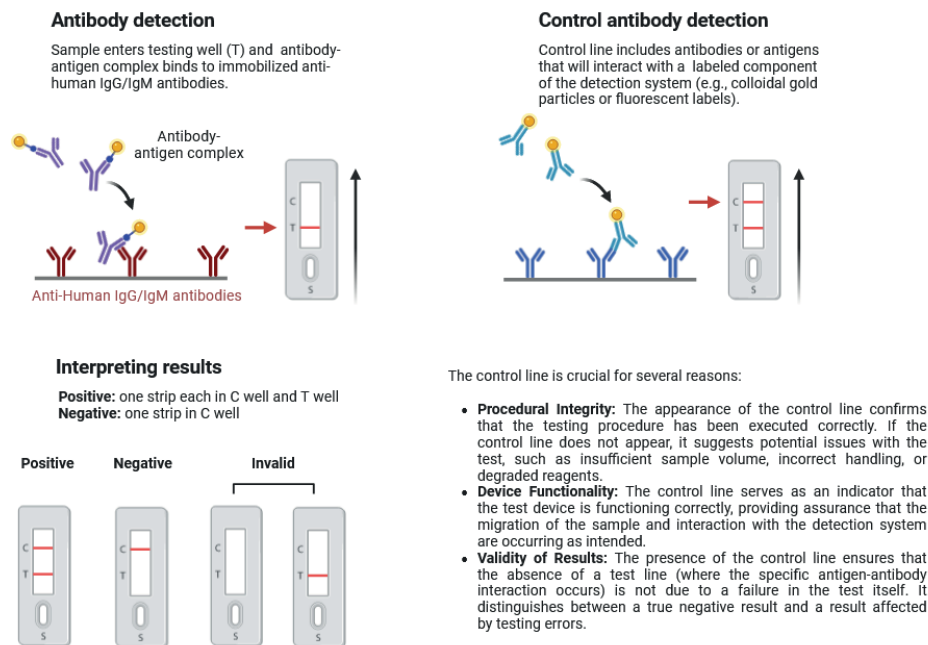
Interpretation and diagnosis: A positive result can be indicative of pneumonia caused by the targeted bacteria, influencing treatment decisions. However, a negative result does not rule out pneumonia entirely, as these tests may not detect all strains or species of the pathogens.

## 5. Comparative Sensitivity and Specificity

The sensitivity and specificity of RDTs compared to traditional methods have been subjects of rigorous evaluation. Legionella urine antigen assays utilize specific capture antibodies for *L.pneumophila* serogroup 1, recognized as the primary cause of Legionnaires' disease (LD). Consequently, these assays demonstrate optimal performance in the context of *L.pneumophila* serogroup 1 infections, exhibiting a combined clinical sensitivity and specificity of 74% and 99%, respectively, for LD, as indicated by a comprehensive meta-analysis [19]. Notably, these sensitivity findings are considerably lower than the individual claims made by each manufacturer. Essentially, the pooled clinical test performance suggests that a positive Legionella antigen test can indicate LD, but a negative result

cannot reliably rule out the diagnosis. However, these assays poorly detect other serogroups of *L. pneumophila* and non-pneumophila *Legionella* species (sensitivity ranging from 5%–40%), potentially leading to an underestimation of the true clinical significance of these organisms [20].

The immunochromatographic (ICT) urinary antigen test is particularly advantageous for detecting pneumococcal pneumonia in situations where obtaining timely cultures is challenging or when antibiotic therapy has already been initiated. In sequential specimens from confirmed bacteremic cases, the ICT assay could still detect the pneumococcal urinary antigen in 83% of the cases even after 3 days of therapy [21]. This form of urinary antigen testing offers key additional benefits, including rapid results (around 15 minutes), simplicity, and reasonable specificity in adults. Studies in adults have demonstrated a sensitivity ranging from 50%–80% and a specificity exceeding 90% [22]. In a specific study, the use of the ICT pneumococcal urinary antigen test increased the rate of identifying the cause of community-acquired pneumonia (CAP) from 39.1%–53.1%. Among 269 patients without a defined etiology using conventional methods, 25.7% showed a positive pneumococcal urinary antigen test. Moreover, the immunochromatography assay is highly accurate



**Figure 1:** Assay principle and visual result interpretation.

in diagnosing pneumococcal meningitis, with a sensitivity of 95% using cerebrospinal fluid and 57% using urine, along with 100% specificity [23].

## 6. Clinical Implementation and Impact

Tests for LD and pneumococcal CAP in urine are quick and easily accessible laboratory methods. These should be integrated into all testing procedures for CAP. Because clinical implementation of RDTs for pneumonia has ushered in a new era of precision and efficiency in patient management [24]. By significantly reducing diagnostic turnaround times, RDTs enable clinicians to swiftly identify the causative agents of pneumonia, allowing for the prompt initiation of targeted treatments. This not only enhances patient outcomes but also contributes to the global effort to combat antibiotic resistance by minimizing the inappropriate use of antibiotics. Furthermore, RDTs play a pivotal role in optimizing healthcare resource utilization, as they reduce the need for extensive laboratory infrastructure and the associated costs. The impact

of these tests is especially notable in critical care settings, where rapid and accurate diagnoses are paramount. As RDTs continue to evolve and become more widely adopted, they are poised to revolutionize pneumonia management, driving improvements in patient care, antimicrobial stewardship, and healthcare efficiency.

## 7. Challenges and Considerations

Despite their numerous advantages, the implementation of RDTs for pneumonia does come with some notable challenges and considerations. One significant challenge is the cost associated with acquiring and maintaining these specialized testing systems, which may limit their accessibility, particularly in resource-constrained healthcare settings [25]. Additionally, the accuracy of RDTs can be influenced by factors like sample quality and timing, necessitating strict adherence to proper testing protocols. Furthermore, the ever-evolving landscape of infectious pathogens poses a challenge for RDT developers to ensure broad



pathogen coverage. Urinary antigen detection tests continue to have significant limitations, including their inability to identify all pneumococcus serotypes and other species of *Legionella* [24]. The interpretation of RDT results also demands a level of expertise, highlighting the need for training and education for healthcare professionals. Moreover, while RDTs can differentiate between viral and bacterial infections to some extent, they may not always provide the full spectrum of information required for precise treatment decisions. These challenges and considerations underscore the importance of carefully evaluating the role of RDTs in pneumonia diagnosis and treatment within the context of each healthcare setting and patient population.

## 8. Future Directions and Innovations

The rapid diagnostic field continues to evolve, with ongoing research focused on refining existing technologies and developing novel approaches. The integration of artificial intelligence and machine learning is poised to enhance diagnostic accuracy further, potentially predicting disease severity and guiding treatment decisions. Well-designed studies are now essential to assess the usefulness of these tests in relation to clinical outcomes. Continued collaboration between researchers, clinicians, and industry stakeholders will shape the future landscape of rapid pneumonia diagnostics.

## 9. Conclusion

In conclusion, RDTs have emerged as game-changers in the management of pneumonia. By offering real-time pathogen identification, these tests contribute to optimized treatment strategies, reduced antibiotic misuse, and improved patient care. As the field advances, it is crucial to address

challenges and maintain a vigilant approach to research, development, and implementation, ultimately ensuring better outcomes for individuals affected by pneumonia. RDTs, strategically integrated into the diagnostic process and selectively utilized for patients who stand to gain the most from these technologies, could serve as a compelling and practical tool. This approach has the potential to enhance the precision of treatment timing, particularly concerning the timely adjustment or cessation of antibiotic therapy.

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