Urine Antigen Tests for the Diagnosis of Respiratory Infections

Legionellosis, Histoplasmosis, Pneumococcal Pneumonia

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KEYWORDS

• Urine antigen tests • *Legionella* • *Histoplasma* • *Streptococcus pneumoniae*

KEY POINTS

- Because of their high specificity, urine antigen tests for *Legionella* and pneumococcus offer rapid pathogen identification for community-acquired pneumonia, allowing for targeted antimicrobial therapy.
- Although the urine antigen test provides many benefits over traditional methods, culture is still required for bacterial antimicrobial susceptibility profiles and epidemiologic data.
- Urinary antigen testing has revolutionized diagnostic testing particularly for disseminated histoplasmosis, largely supplanting serology.
- Recent commercial development of *Histoplasma* urine antigen reagents may allow institutions to perform testing in-house as an alternative to submitting specimens to reference laboratories.

INTRODUCTION

Diagnosing respiratory infections has historically relied on targeted culture of respiratory pathogens. Although this can provide adequate sensitivity for some organisms, not all causative organisms can be readily cultured from respiratory specimens. In addition, significant delays in turnaround time (TAT) are detrimental to patient care, particularly in the cases of pneumonia or severely immunocompromised hosts. As a

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result of these limitations, testing for pneumonia has evolved in recent decades to include so-called rapid culture-independent methods. However, not all modalities of culture-independent testing have measured up to clinical expectations. For instance, in the case of direct fluorescence antibody staining for *Legionella pneumophila*, the method has proved to be considerably less sensitive than conventionally used culture methods despite its shortened TAT.[1] In this case, the lack of result accuracy negates the rapidity of the result.

Urinary antigen testing has grown in popularity for several significant respiratory infections, particularly *Legionella pneumophila*, *Streptococcus pneumoniae*, and *Histoplasma capsulatum*. The broad concept of urinary antigen testing capitalizes on the concentration of shed antigen from a variety of pathogens in the kidneys for excretion in the urine. The antigens are then detected via an immunoassay such as an enzyme-linked immunosorbent assay (ELISA) or an immunochromatographic or lateral flow assay (LFA). Of importance is that the aforementioned pathogens are not present in the urine for culture, despite the target antigen being concentrated on this anatomic site. This situation allows for a noninvasive specimen collection to provide information on an infection occurring in a distal anatomic location. Urinary antigen testing can therefore be used to obtain rapid test results related to respiratory infection, independent of an invasive collection such as a bronchoalveolar lavage (BAL). This article describes the 3 aforementioned organisms, their role in respiratory disease, and the current status of urinary antigen testing in their respective diagnosis.

MICROBIOLOGY

Legionella

Legionella spp are fastidious, gram-negative bacilli that are ubiquitous in the aqueous environment, often parasitizing free-living amoebas.[2] The unusual nutritional requirements of this organism has led to a general difficulty in recovering the organism in many clinical cases of respiratory infections, with average cultures requiring 2 to 5 days for growth. While up to one-third of the validly named species have been isolated from humans, *L pneumophila* is conventionally considered the most clinically significant species, and within this species serogroup 1 is considered the most significant.[3]

Pneumococcus

S pneumoniae is a gram-positive coccus and a member of the viridans group of streptococcal bacteria. The pneumococcal genome is approximately 2 million base pairs, with more than 150 genes dedicated to virulence.[4] Pneumococci have to strike a balance between immune evasion and successful colonization of the human nasopharyngeal tract. To do this, they retain the ability to switch between thin, procolonization, polysaccharide capsules and more virulent, thicker capsules.[5,6] Prior colonization with certain bacteria or viral infection can also have dramatic effects on both propneumococcal and antipneumococcal colonization.[7,8]

Histoplasma

H capsulatum is a dimorphic mold of the Ascomycota phylum, Onygenales order. This organism exists in the body as a small, intracellular yeast (2–4 μm), exhibiting narrow-based budding, and in the environment as a mold with hyphae, tuberculate macroconidia, and smooth microconidia.[9] Environmentally, (+) and (−) forms of the perfect state (*Ajellomyces capsulatus*) combine sexually,[10] whereas replication in vivo transpires asexually by budding.