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- Infections in Patients with Cystic Fibrosis: Diagnostic Microbiology Update** 197
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- Survival has improved in patients with cystic fibrosis (CF), in part because of aggressive antimicrobial management. Two multidrug-resistant environmental bacteria, the *Burkholderia cepacia* group and nontuberculous mycobacteria, have emerged. Improving genomic and proteomic technologies are allowing better identification of bacteria and fungi found in the CF lung and detection of viral agents that may be associated with pulmonary exacerbations. Anaerobic bacteria and *Streptococcus anginosus* group organisms may play a role in chronic CF lung infections. The diversity of organisms declines perhaps as a result of aggressive antimicrobial therapy, and an apex predator, *Pseudomonas aeruginosa*, may emerge in many patients with CF.
- Urine Antigen Tests for the Diagnosis of Respiratory Infections: Legionellosis, Histoplasmosis, Pneumococcal Pneumonia** 219
 Marc Roger Couturier, Erin H. Graf, and Allen T. Griffin
- Urinary antigen testing has grown in popularity for several significant respiratory infections, particularly *Legionella pneumophila*, *Streptococcus pneumoniae*, and *Histoplasma capsulatum*. By capitalizing on the concentration of shed antigen from a variety of pathogens in the kidneys for excretion in the urine, urinary antigen testing can be used to obtain rapid test results related to respiratory infection, independent of an invasive collection such as a bronchoalveolar lavage. This article describes the 3 aforementioned organisms, their role in respiratory disease, and the current status of urinary antigen testing in their respective diagnosis.
- Pertussis: Relevant Species and Diagnostic Update** 237
 Amy L. Leber
- Pertussis is increasing due to multiple factors including increasing awareness by clinicians, decreased effectiveness of vaccines, and improved testing. While *Bordetella pertussis* is the causative agent of pertussis other *Bordetella* species such as *B. parapertussis*, and *B. holmesii*, have been associated with pertussis-like illness. Laboratory diagnosis is made using various tests with molecular methods supplanting culture due to increased sensitivity. Serology is useful but standardized methods that are needed. The targets used for molecular detection are varied and have differing sensitivities and specificities. Laboratorians must consider if differentiation of various *Bordetella* species is necessary when choosing an amplified testing approach.

Antibiotic Resistance in Nosocomial Respiratory Infections

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Gerald A. Denys and Ryan F. Relich

Nosocomial respiratory infections are the most common acquired infections in patients with severe underlying conditions and are responsible for high morbidity and mortality in this patient population. Multidrug-resistant (MDR) pathogens are associated with hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP). This article describes the etiology, epidemiology, pathogenesis, diagnosis, and treatment of HAP and VAP associated with antibiotic-resistant bacterial pathogens.

Nontuberculous Mycobacteria in Respiratory Infections: Advances in Diagnosis and Identification

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Akos Somoskovi and Max Salfinger

An urgent question that needs to be addressed rapidly by the mycobacteriology laboratory is whether *Mycobacterium tuberculosis* complex or NTM is involved. NAA assays are excellent tools for the purpose, and can be used directly on the clinical specimens of patients suspected of having mycobacterial disease, allowing same-day reporting of results. The CDC recommends using both liquid and solid media for growth detection of mycobacteria to decrease the time to detection and to increase the yield of growth detection. DNA sequencing of variable genomic regions offers a rapid, accurate, and relatively inexpensive method for the identification of mycobacteria.

Molecular Diagnosis of Tuberculosis and Drug Resistance

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Shou-Yean Grace Lin and Edward P. Desmond

Molecular drug susceptibility testing (MDST) provides rapid diagnosis of tuberculosis (TB) and detection of drug resistance with commendable sensitivity and specificity. MDST reduces unnecessary isolation or treatment, when a negative result for TB is obtained. Because of the possibility of false detection of rifampin resistance by probe-based MDST, confirmation by sequencing is recommended, especially in regions where the prevalence of resistance is low. Revealing mutation identity by sequencing offers opportunities to study drug minimum inhibitory concentrations for each mutation. Such information enables prediction of resistance levels, and may be helpful in formulating optimal regimens, when treatment options are limited.

Nonmolecular Methods for the Diagnosis of Respiratory Fungal Infections

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Frédéric Lamoth and Barbara D. Alexander

Diagnosis of invasive fungal pneumonias by conventional culture methods is difficult to assess and often delayed. Nonmolecular fungal markers have emerged as an important adjunctive tool to support their diagnosis in combination with other clinical, radiologic, and microbiological criteria of invasive fungal diseases. Concerns about the sensitivity and specificity of some tests in different patient populations should lead to warnings about their widespread use. None can identify the emerging and particularly deadly fungal pathogens responsible for mucormycosis. The role of non-molecular fungal markers should be better defined in combination with

other microbiological and radiologic tools in preemptive antifungal strategies.

Interferon-Gamma Release Assays

337

Robert Belknap and Charles L. Daley

Diagnosis of latent tuberculosis infection (LTBI) should be targeted toward individuals and groups with high risk of progression to active tuberculosis (TB). Low-risk populations should not be screened. Interferon-gamma release assays (IGRAs) perform as well or better than the tuberculin skin test in most targeted populations. IGRAs are preferred for bacille Calmette-Guérin (BCG)-vaccinated populations. A positive IGRA in a person at low risk for TB exposure should be confirmed with a repeat test or another method before recommending LTBI treatment. The choice of which IGRA to use is generally based on the costs and feasibility of performing the test.

Respiratory Fungal Infections: Molecular Diagnostic Tests

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Kevin C. Hazen

Fungal infection of the respiratory tract can take several forms, the most common of which is pneumonia. Fungal infection can occur in the immunocompetent typically as a result of inhalation of a large inoculum of fungal elements. However, the number of etiologic agents attacking immunocompetent individuals and causing significant infection is limited. Molecular assays are a potential additional and sensitive weapon that can be added to the diagnostic arsenal used by physicians to determine whether a fungus is definitively, probably, or possibly causing infection in a patient.

Rapid Diagnosis of Influenza: State of the Art

365

David R. Peaper and Marie L. Landry

Much effort has been expended developing testing modalities for influenza viruses that are capable of providing rapid results to clinicians. Antigen-detection techniques, historically the only methods able to deliver results quickly, are still widely used despite concerns about sensitivity. Recently, nucleic acid amplification tests (NAATs), which can achieve rapid turnaround times and high sensitivity, have become available. In addition, NAATs can detect other respiratory pathogens. Although there are many theoretical advantages to rapid influenza testing, the clinical impact of testing in various patient populations must be considered against the cost and the analytical performance of the tests.

Antiviral Resistance in Influenza Viruses: Laboratory Testing

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Jennifer Laplante and Kirsten St. George

Influenza continues to be a significant health care issue. Although vaccination is the major line of defense, antiviral drugs play an important role in prophylaxis and disease management. Approved drugs for influenza are currently limited to those that target the viral matrix protein or neuraminidase enzyme. Resistance-associated sequence changes in the genes encoding these proteins have been extensively studied. Available methods

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for genotypic and phenotypic antiviral susceptibility testing have expanded and are being further developed and improved. The sporadic emergence of drug-resistant variants and the global spread of resistant strains have demonstrated the ongoing need for vigilant testing and surveillance.

Emerging Respiratory Viruses Other than Influenza

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James J. Dunn and Melissa B. Miller

Non-influenza respiratory virus infections are common worldwide and contribute to morbidity and mortality in all age groups. The recently identified Middle East respiratory syndrome coronavirus has been associated with rapidly progressive pneumonia and high mortality rate. Adenovirus 14 has been increasingly recognized in severe acute respiratory illness in both military and civilian individuals. Rhinovirus C and human bocavirus type 1 have been commonly detected in infants and young children with respiratory tract infection and studies have shown a positive correlation between respiratory illness and high viral loads, mono-infection, viremia, and/or serologically-confirmed primary infection.

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