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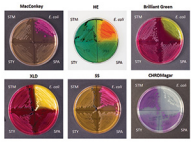
COVER IMAGE



Cover photograph: Comparison of three *Salmonella enterica* serovars and *Escherichia coli* on selective agar plates. *E. coli* strain R27 (*E. coli*), *Salmonella enterica* serovar Typhimurium strain SL1344 (STM), *Salmonella enterica* serovar Typhi strain CT18 (STY), and *Salmonella enterica* serovar Paratyphi A strain 45157 (SPA) were streaked on six selective agar medium plates routinely used for laboratory diagnostics of *Salmonella*. The selective plates included MacConkey, Hektoen enteric (HE), brilliant green, xylose lysine deoxycholate (XLD), *Salmonella Shigella* (SS), and CHROMagar *Salmonella* Plus agar media. Following incubation at 37°C, bacterial growth and colony pigmentation were imaged using a Pentax K-5 camera. (Photographs by Ohad Gal-Mor and Yakov Levit.) *(See related article at e00088-18.)*

ACKNOWLEDGMENT OF REVIEWERS

PRACTICAL GUIDANCE FOR CLINICAL MICROBIOLOGY

Summary: Respiratory viral infections are associated with a wide range of acute syndromes and infectious disease processes in children and adults worldwide. Many viruses are implicated in these infections, and these viruses are spread largely via respiratory means between humans but also occasionally from animals to humans. This article is an American Society for Microbiology (ASM)-sponsored Practical Guidance for Clinical Microbiology (PGCM) document identifying best practices for diagnosis and characterization of viruses that cause acute respiratory infections and replaces the most recent prior version of the ASM-sponsored Cumitech 21 document, *Laboratory Diagnosis of Viral Respiratory Disease*, published in 1986. The scope of the original document was quite broad, with an emphasis on clinical diagnosis of a wide variety of infectious agents and laboratory focus on antigen detection and viral culture. The new PGCM document is designed to be used by laboratorians in a wide variety of diagnostic and public health microbiology/virology laboratory settings worldwide. The article provides guidance to a rapidly changing field of diagnostics and outlines the epidemiology and clinical impact of acute respiratory viral infections, including preferred methods of specimen collection and current methods for diagnosis and characterization of viral pathogens causing acute respiratory tract infections. Compared to the case in 1986, molecular techniques are now the preferred diagnostic approaches for the detection of acute respiratory viruses, and they allow for automation, high-throughput workflows, and near-patient testing. These changes require quality assurance programs to prevent laboratory contamination as well as strong preanalytical screening approaches to utilize laboratory resources appropriately. Appropriate guidance from laboratorians to stakeholders will allow for appropriate specimen collection, as well as correct test ordering that will quickly identify highly transmissible emerging pathogens.

Instructions to Authors are available on the journal website.

REVIEWS

Summary: Matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) has been successfully applied in recent years for first-line identification of pathogens in clinical microbiology because it is simple to use, rapid, and accurate and has economic benefits in hospital management. The range of clinical applications of MALDI-TOF MS for bacterial isolates is increasing constantly, from species identification to the two most promising applications in the near future: detection of antimicrobial resistance and strain typing for epidemiological studies. The aim of this review is to outline the contribution of previous MALDI-TOF MS studies in relation to detection of antimicrobial resistance and to discuss potential future challenges in this field. Three main approaches are ready (or almost ready) for clinical use, including the detection of antibiotic modifications due to the enzymatic activity of bacteria, the detection of antimicrobial resistance by analysis of the peak patterns of bacteria or mass peak profiles, and the detection of resistance by semiquantification of bacterial growth in the presence of a given antibiotic. This review provides an expert guide for MALDI-TOF MS users to new approaches in the field of antimicrobial resistance detection, especially possible applications as a routine diagnostic tool in microbiology laboratories.

Summary: HIV diagnostics have played a central role in the remarkable progress in identifying, staging, initiating, and monitoring infected individuals on life-saving antiretroviral therapy. They are also useful in surveillance and outbreak responses, allowing for assessment of disease burden and identification of vulnerable populations and transmission "hot spots," thus enabling planning, appropriate interventions, and allocation of appropriate funding. HIV diagnostics are critical in achieving epidemic control and require a hybrid of conventional laboratory-based diagnostic tests and new technologies, including point-of-care (POC) testing, to expand coverage, increase access, and positively impact patient management. In this review, we provide (i) a historical perspective on the evolution of HIV diagnostics (serologic and molecular) and their interplay with WHO normative guidelines, (ii) a description of the role of conventional and POC testing within the tiered laboratory diagnostic network, (iii) information on the evaluations and selection of appropriate diagnostics, (iv) a description of the quality management systems needed to ensure reliability of testing, and (v) strategies to increase access while reducing the time to return results to patients. Maintaining the central role of HIV diagnostics in programs requires periodic monitoring and optimization with quality assurance in order to inform adjustments or alignment to achieve epidemic control.

Summary: Humans encounter mycobacterial species due to their ubiquity in different environmental niches. In many individuals, pathogenic mycobacterial species may breach our first-line barrier defenses of the innate immune system and modulate the activation of phagocytes to cause disease of the respiratory tract or the skin and soft

tissues, sometimes resulting in disseminated infection. Cutaneous mycobacterial infections may cause a wide range of clinical manifestations, which are divided into four main disease categories: (i) cutaneous manifestations of *Mycobacterium tuberculosis* infection, (ii) Buruli ulcer caused by *Mycobacterium ulcerans* and other related slowly growing mycobacteria, (iii) leprosy caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis*, and (iv) cutaneous infections caused by rapidly growing mycobacteria. Clinically, cutaneous mycobacterial infections present with widely different clinical presentations, including cellulitis, nonhealing ulcers, subacute or chronic nodular lesions, abscesses, superficial lymphadenitis, verrucous lesions, and other types of findings. Mycobacterial infections of the skin and subcutaneous tissue are associated with important stigma, deformity, and disability. Geography-based environmental exposures influence the epidemiology of cutaneous mycobacterial infections. Cutaneous tuberculosis exhibits different clinical phenotypes acquired through different routes, including via extrinsic inoculation of the tuberculous bacilli and dissemination to the skin from other sites, or represents hypersensitivity reactions to *M. tuberculosis* infection. In many settings, leprosy remains an important cause of neurological impairment, deformity, limb loss, and stigma. *Mycobacterium lepromatosis*, a mycobacterial species related to *M. leprae*, is linked to diffuse lepromatous leprosy of Lucio and Latapí. *Mycobacterium ulcerans* produces a mycolactone toxin that leads to subcutaneous tissue destruction and immunosuppression, resulting in deep ulcerations that often produce substantial disfigurement and disability. *Mycobacterium marinum*, a close relative of *M. ulcerans*, is an important cause of cutaneous sporotrichoid nodular lymphangitic lesions. Among patients with advanced immunosuppression, *Mycobacterium kansasii*, the *Mycobacterium avium-intracellulare* complex, and *Mycobacterium haemophilum* may cause cutaneous or disseminated disease. Rapidly growing mycobacteria, including the *Mycobacterium abscessus* group, *Mycobacterium chelonei*, and *Mycobacterium fortuitum*, are increasingly recognized pathogens in cutaneous infections associated particularly with plastic surgery and cosmetic procedures. Skin biopsies of cutaneous lesions to identify acid-fast staining bacilli and cultures represent the cornerstone of diagnosis. Additionally, histopathological evaluation of skin biopsy specimens may be useful in identifying leprosy, Buruli ulcer, and cutaneous tuberculosis. Molecular assays are useful in some cases. The treatment for cutaneous mycobacterial infections depends on the specific pathogen and therefore requires a careful consideration of antimicrobial choices based on official treatment guidelines.

Summary: The ability of pathogenic bacteria to affect higher organisms and cause disease is one of the most dramatic properties of microorganisms. Some pathogens can establish transient colonization only, but others are capable of infecting their host for many years or even for a lifetime. Long-term infection is called persistence, and this phenotype is fundamental for the biology of important human pathogens, including *Helicobacter pylori*, *Mycobacterium tuberculosis*, and *Salmonella enterica*. Both typhoidal and nontyphoidal serovars of the species *Salmonella enterica* can cause persistent infection in humans; however, as these two *Salmonella* groups cause clinically distinct diseases, the characteristics of their persistent infections in humans differ significantly. Here, following a general summary of *Salmonella* pathogenicity, host specificity, epidemiology, and laboratory diagnosis, I review the current knowledge about *Salmonella* persistence and discuss the relevant epidemiology of persistence (including carrier rate, duration of shedding, and host and pathogen risk factors), the host response to *Salmonella* persistence, *Salmonella* genes involved in this lifestyle, as well

Summary: The tick-borne pathogen Powassan virus is a rare cause of encephalitis in North America and the Russian Far East. The number of documented cases described since the discovery of Powassan virus in 1958 may be <150, although detection of cases has increased over the past decade. In the United States, the incidence of Powassan virus infections expanded from the estimated 1 case per year prior to 2005 to 10 cases per year during the subsequent decade. The increased detection rate may be associated with several factors, including enhanced surveillance, the availability of improved laboratory diagnostic methods, the expansion of the vector population, and, perhaps, altered human activities that lead to more exposure. Nonetheless, it remains unclear whether Powassan virus is indeed an emerging threat or if enzootic cycles in nature remain more-or-less stable with periodic fluctuations of host and vector population sizes. Despite the low disease incidence, the approximately 10% to 15% case fatality rate of neuroinvasive Powassan virus infection and the temporary or prolonged sequelae in >50% of survivors make Powassan virus a medical concern requiring the attention of public health authorities and clinicians. The medical importance of Powassan virus justifies more research on developing specific and effective treatments and prevention and control measures.