COVER IMAGE

Cover photograph: Scanning electron micrograph of the Houston-1 strain of Bartonella henselae exhibiting in vitro biofilm growth. The image shows adherent bacteria grown for 72 h directly on a cellulose membrane. The inset (red) image shows individual bacilli visible in the extracellular polymeric substance (EPS) of the biofilm. Secondary images were collected as JPEGs and pseudocolorized based on pixel intensity using Image J and Adobe Photoshop. (See related article on page 709.) (Copyright © 2017 American Society for Microbiology. All Rights Reserved.)

REVIEWS

Bacterial and Fungal Endophthalmitis

Marlene L. Durand

Summary: Endophthalmitis is a severe eye infection that may result in permanent loss of useful vision in the affected eye. Most cases are exogenous and occur as a complication of cataract surgery, an intravitreal injection, or penetrating ocular trauma. Endogenous endophthalmitis results from hematogenous seeding of the eye by bacteria or fungi, but bacteremia or fungemia may be transient and patients may present without symptoms of systemic infection. Nearly all endophthalmitis patients present with decreased vision, and some also have eye pain. Eye examination usually reveals a hypopyon and intraocular inflammation. Diagnosis is clinical, supported by cultures of the vitreous and/or aqueous or by blood cultures in some endogenous cases. Molecular diagnostic techniques have been used in research laboratories for pathogen identification in endophthalmitis and offer the possibility of rapid diagnosis, including in culture-negative cases. Intravitreal injection of antibiotics is the most important component of treatment; some cases also benefit from surgical debridement of the vitreous by a vitrectomy. The visual outcome depends partly on the pathogen: coagulase-negative staphylococcal endophthalmitis has a better prognosis than does streptococcal endophthalmitis, for example. Endophthalmitis is a medical emergency, and prompt diagnosis and treatment are essential for saving vision.

Toxoplasma Effectors Targeting Host Signaling and Transcription

Mohamed-Ali Hakimi, Philipp Olias, L. David Sibley

Summary: Early electron microscopy studies revealed the elaborate cellular features that define the unique adaptations of apicomplexan parasites. Among these were bulbous rhoptry (ROP) organelles and small, dense granules (GRAs), both of which are secreted during invasion of host cells. These early morphological studies were followed by the exploration of the cellular contents of these secretory organelles, revealing them to be comprised of highly divergent protein families with few conserved domains or predicted functions. In parallel, studies on host-pathogen interactions identified many host signaling pathways that were mysteriously altered by infection. It was only with the advent of forward and reverse genetic strategies that the connections between individual parasite effectors and the specific host pathways that they targeted finally became clear. The current repertoire of parasite effectors includes ROP kinases and pseudokinases that are secreted during invasion and that block host immune pathways. Similarly, many secretory GRA proteins alter host gene expression by activating host transcription factors, through modification of chromatin, or by inducing small noncoding RNAs. These effectors highlight novel mechanisms by which T. gondii has learned to harness host signaling to favor intracellular survival and will guide future studies designed to uncover the additional complexity of this intricate host-pathogen interaction.

Instructions to Authors are available at http://journalitas.asm.org/t/49539.
Susceptibility Testing of Medically Important Parasites

Abebe Genetu Bayih, Anjan Debnath, Edward Mitre, Christopher D. Huston, Benoit Lalou, Didier Leroy, Benjamin Blasco, Brice Campo, Timothy N. C. Wells, Paul A. Willis, Peter Sjö, Wesley C. Van Voorhis, Dylan R. Pillai

Summary: In the last 2 decades, renewed attention to neglected tropical diseases (NTDs) has spurred the development of antiparasitic agents, especially in light of emerging drug resistance. The need for new drugs has required in vitro screening methods using parasite culture. Furthermore, clinical laboratories sought to correlate in vitro susceptibility methods with treatment outcomes, most notably with malaria. Parasites with their various life cycles present greater complexity than bacteria, for which standardized susceptibility methods exist. This review catalogs the state-of-the-art methodologies used to evaluate the effects of drugs on key human parasites from the point of view of drug discovery as well as the need for laboratory methods that correlate with clinical outcomes.

Investigating Clinical Issues by Genotyping of Medically Important Fungi: Why and How?

Alexandre Alanio, Marie Desnos-Ollivier, Dea Garcia-Hermoso, Stéphane Bretagne

Summary: Genotyping studies of medically important fungi have addressed elucidation of outbreaks, nosocomial transmissions, infection routes, and genotype-phenotype correlations, of which secondary resistance has been most intensively investigated. Two methods have emerged because of their high discriminatory power and reproducibility: multilocus sequence typing (MLST) and microsatellite length polymorphism (MLP) using short tandem repeat (STR) markers. MLST relies on single-nucleotide polymorphisms within the coding regions of housekeeping genes. STR polymorphisms are based on the number of repeats of short DNA fragments, mostly outside coding regions, and thus are expected to be more polymorphic and more rapidly evolving than MLST markers. There is no consensus on a universal typing system. Either one or both of these approaches are now available for Candida spp., Aspergillus spp., Fusarium spp., Scedosporium spp., Cryptococcus neoformans, Pneumocystis jirovecii, and endemic mycoses. The choice of the method and the number of loci to be tested depend on the clinical question being addressed. Next-generation sequencing is becoming the most appropriate method for fungi with no MLP or MLST typing available. Whatever the molecular tool used, collection of clinical data (e.g., time of hospitalization and sharing of similar rooms) is mandatory for investigating outbreaks and nosocomial transmission.

Bartonella Species, an Emerging Cause of Blood-Culture-Negative Endocarditis

Udoka Okaro, Anteneh Addisu, Beata Casanas, Burt Anderson

Summary: Since the reclassification of the genus Bartonella in 1993, the number of species has grown from 1 to 45 currently designated members. Likewise, the association of different Bartonella species with human disease continues to grow, as does the range of clinical presentations associated with these bacteria. Among these, blood-culture-negative endocarditis stands out as a common, often undiagnosed, clinical presentation of infection with several different Bartonella species. The limitations of laboratory tests resulting in this underdiagnosis of Bartonella endocarditis are discussed. The varied clinical picture of Bartonella infection and a review of clinical aspects of endocarditis caused by Bartonella are presented. We also summarize the current knowledge of the molecular basis of Bartonella pathogenesis, focusing on surface adhesins in the two Bartonella species that most commonly cause endocarditis, B. henselae and B. quintana. We discuss evidence that surface adhesins are important factors for autoaggregation and biofilm formation by Bartonella species. Finally, we propose that biofilm formation is a critical step in the formation of vegetative masses during Bartonella-mediated endocarditis and represents a potential reservoir for persistence by these bacteria.
**Mycoplasma pneumoniae** from the Respiratory Tract and Beyond

Ken B. Waites, Li Xiao, Yang Liu, Mitchell F. Balish, T. Prescott Atkinson

Summary: *Mycoplasma pneumoniae* is an important cause of respiratory tract infections in children as well as adults that can range in severity from mild to life-threatening. Over the past several years there has been much new information published concerning infections caused by this organism. New molecular-based tests for *M. pneumoniae* detection are now commercially available in the United States, and advances in molecular typing systems have enhanced understanding of the epidemiology of infections. More strains have had their entire genome sequences published, providing additional insights into pathogenic mechanisms. Clinically significant acquired macrolide resistance has emerged worldwide and is now complicating treatment. In vitro susceptibility testing methods have been standardized, and several new drugs that may be effective against this organism are undergoing development. This review focuses on the many new developments that have occurred over the past several years that enhance our understanding of this microbe, which is among the smallest bacterial pathogens but one of great clinical importance.

Strategies for Prevention and Treatment of *Trichomonas vaginalis* Infections

Kawthar Bouchemal, Christian Bories, Philippe M. Loiseau

Summary: The last estimated annual incidence of *Trichomonas vaginalis* worldwide exceeds that of chlamydia and gonorrhea combined. This critical review updates the state of the art on advances in *T. vaginalis* diagnostics and strategies for treatment and prevention of trichomoniasis. In particular, new data on treatment outcomes for topical administration of formulations are reviewed and discussed.

Current and Emerging Topical Antibacterials and Antiseptics: Agents, Action, and Resistance Patterns

Deborah A. Williamson, Glen P. Carter, Benjamin P. Howden

Summary: Bacterial skin infections represent some of the most common infectious diseases globally. Prevention and treatment of skin infections can involve application of a topical antimicrobial, which may be an antibiotic (such as mupirocin or fusidic acid) or an antiseptic (such as chlorhexidine or alcohol). However, there is limited evidence to support the widespread prophylactic or therapeutic use of topical agents. Challenges involved in the use of topical antimicrobials include increasing rates of bacterial resistance, local hypersensitivity reactions (particularly to older agents, such as bacitracin), and concerns about the indiscriminate use of antiseptics potentially coselecting for antibiotic resistance. We review the evidence for the major clinical uses of topical antibiotics and antiseptics. In addition, we review the mechanisms of action of common topical agents and define the clinical and molecular epidemiology of antimicrobial resistance in these agents. Moreover, we review the potential use of newer and emerging agents, such as retapamulin and ebselen, and discuss the role of antiseptic agents in preventing bacterial skin infections. A comprehensive understanding of the clinical efficacy and drivers of resistance to topical agents will inform the optimal use of these agents to preserve their activity in the future.