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Nonculture Methods for Diagnosis of Disseminated Candidiasis. 311-323
Errol Reiss and Christine J. Morrison.....

Summary: Nonculture methods to diagnose disseminated candidiasis (DC) are needed because blood cultures are nonproductive for 27% or more of patients with DC. Recent reports indicate the emergence of Candida (Torulopsis) glabrata, Candida parapsilosis, and Candida krusei as agents of DC in addition to Candida albicans and Candida tropicalis. The Candida species metabolite D-arabinitol, expressed as serum D-arabinitol/creatinine, is an indicator of DC in as many as two-thirds of patients studied. Detection is expedited by an enzymatic-fluorometric assay kit as an alternative to gas-liquid chromatography, but interference from mannitol may detract from test specificity. Polymerase chain reaction (PCR)-amplified Candida species DNA has been recovered from blood and urine samples from a small number of human subjects. PCR-based tests are promising but cumbersome prototypes. The sensitivity to detect 1 to 10 CFU/ml of blood has not been reliably achieved. Immunoassay detection of marker antigens for DC has proceeded on several fronts. A liposomal immunoassay kit for the 48-kDa enolase received a successful prospective clinical evaluation. Secreted aspartyl proteinase was detected in urine from immunosuppressed rabbits with DC, but data on human subjects are unavailable. Western blot (immunoblot) was used to detect antigenuria, and this method appears promising. The cell wall mannoprotein (mannan) of Candida species circulates in the low nanogram-per-milliliter range in DC, but frequent sampling is needed for detection during granulocytopenia. The incorporation in the sandwich enzyme immunoassay of antibodies of broad specificity, reflecting the epitopes of C. albicans and the mannan of emerging Candida species, is necessary for maximal sensitivity.

Bacillus cereus and Related Species. Francis A. Drobniowski 324-338

Summary: Bacillus cereus is a gram-positive aerobic or facultatively anaerobic spore-forming rod. It is a cause of food poisoning, which is frequently associated with the consumption of rice-based dishes. The organism produces an emetic or diarrheal syndrome induced by an emetic toxin and enterotoxin, respectively. Other toxins are produced during growth, including phospholipases, proteases, and hemolysins, one of which, cereolysin, is a thiol-activated hemolysin. These toxins may contribute to the pathogenicity of B. cereus in nongastrointestinal disease. B. cereus isolated from

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clinical material other than feces or vomitus was commonly dismissed as a contaminant, but increasingly it is being recognized as a species with pathogenic potential. It is now recognized as an infrequent cause of serious nongastrointestinal infection, particularly in drug addicts, the immunosuppressed, neonates, and postsurgical patients, especially when prosthetic implants such as ventricular shunts are inserted. Ocular infections are the commonest types of severe infection, including endophthalmitis, panophthalmitis, and keratitis, usually with the characteristic formation of corneal ring abscesses. Even with prompt surgical and antimicrobial agent treatment, enucleation of the eye and blindness are common sequelae. Septicemia, meningitis, endocarditis, osteomyelitis, and surgical and traumatic wound infections are other manifestations of severe disease. *B. cereus* produces beta-lactamases, unlike *Bacillus anthracis*, and so is resistant to beta-lactam antibiotics; it is usually susceptible to treatment with clindamycin, vancomycin, gentamicin, chloramphenicol, and erythromycin. Simultaneous therapy via multiple routes may be required.

Human Immunodeficiency Virus Type 1 Infection of the Brain. Walter J. Atwood, Joseph R. Berger, Richard Kaderman, Carlo S. Tornatore, and Eugene O. Major..... 339-366

Summary: Direct infection of the central nervous system by human immunodeficiency virus type 1 (HIV-1), the causative agent of AIDS, was not appreciated in the early years of the AIDS epidemic. Neurological complications associated with AIDS were largely attributed to opportunistic infections that arose as a result of the immunocompromised state of the patient and to depression. In 1985, several groups succeeded in isolating HIV-1 directly from brain tissue. Also that year, the viral genome was completely sequenced, and HIV-1 was found to belong to a neurotropic subfamily of retrovirus known as the Lentivirinae. These findings clearly indicated that direct HIV-1 infection of the central nervous system played a role in the development of AIDS-related neurological disease. This review summarizes the clinical manifestations of HIV-1 infection of the central nervous system and the related neuropathology, the tropism of HIV-1 for specific cell types both within and outside of the nervous system, the possible mechanisms by which HIV-1 damages the nervous system, and the current strategies for diagnosis and treatment of HIV-1-associated neuropathology.

Antifungal Susceptibility Testing. John H. Rex, Michael A. Pfaller, Michael G. Rinaldi, Anamarie Polak, and John N. Galgiani 367-381

*Summary: Unlike antibacterial susceptibility testing, reliable antifungal susceptibility testing is still largely in its infancy. Many methods have been described, but they produce widely discrepant results unless such factors as pH, inoculum size, medium formulation, incubation time, and incubation temperature are carefully controlled. Even when laboratories agree upon a common method, interlaboratory agreement may be poor. As a result of numerous collaborative projects carried out both independently and under the aegis of the Subcommittee on Antifungal Susceptibility Testing of the National Committee for Clinical Laboratory Standards, the effects of varying these factors have been extensively studied and a standard method which minimizes interlaboratory variability during the testing of *Candida* spp. and *Cryptococcus neoformans* has been proposed. This review summarizes this work, reviews the strengths and weaknesses of the proposed susceptibility testing standard, and identifies directions for future work.*

Epidemiologic Evidence for Multiple Sclerosis as an Infection. John F. Kurtzke 382-427

Summary: The worldwide distribution of multiple sclerosis (MS) can be described within three zones of frequency: high, medium, and low. The disease has a predilection for white races and for women. Migration studies show that changing residence changes MS risk. Studies of persons moving from high- to low-risk areas indicate that in the

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high-risk areas. MS is acquired by about age 15. Moves from low- to high-risk areas suggest that susceptibility is limited to persons between about ages 11 and 45. MS on the Faroe Islands has occurred as four successive epidemics beginning in 1943. The disease appears to have been introduced by British troops who occupied the islands for 5 years from 1940, and it has remained geographically localized within the Faroes for half a century. What was introduced must have been an infection, called the primary MS affection (PMSA), that was spread to and from successive cohorts of Faroese. In this concept, PMSA is a single widespread systemic infectious disease (perhaps asymptomatic) that only seldom leads to clinical neurologic MS. PMSA is also characterized by a need for prolonged exposure, limited age of susceptibility, and prolonged incubation. I believe that clinical MS is the rare late outcome of a specific, but unknown, infectious disease of adolescence and young adulthood and that this infection could well be caused by a thus-far-unidentified (retro)virus.

An Overview of Nosocomial Infections, Including the Role of the Microbiology Laboratory. T. Grace Emori and Robert P. Gaynes..... 428-442

Summary: An estimated 2 million patients develop nosocomial infections in the United States annually. The increasing number of antimicrobial agent-resistant pathogens and high-risk patients in hospitals are challenges to progress in preventing and controlling these infections. While Escherichia coli and Staphylococcus aureus remain the most common pathogens isolated overall from nosocomial infections, coagulase-negative staphylococci (CoNS), organisms previously considered contaminants in most cultures, are now the predominant pathogens in bloodstream infections. The growing number of antimicrobial agent-resistant organisms is troublesome, particularly vancomycin-resistant CoNS and Enterococcus spp. and Pseudomonas aeruginosa resistant to imipenem. The active involvement and cooperation of the microbiology laboratory are important to the infection control program, particularly in surveillance and the use of laboratory services for epidemiologic purposes. Surveillance is used to identify possible infection problems, monitor infection trends, and assess the quality of care in the hospital. It requires high-quality laboratory data that are timely and easily accessible.

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