Mixed Viral Infections: Detection and Management. Joseph L. Waner

Summary: An analysis was done of the incidence and nature of mixed virus infections diagnosed in the same clinical specimen from immunocompetent patients; respiratory viruses were emphasized. Few studies have addressed mixed viral infections in any systematic fashion. The relevant studies reviewed focused on clinical relationships or diagnostic methods. Data relating to multiple infections were usually derived incidentally to the purpose of the investigations. Sixty-three percent of the reports with data on mixed infections identified them in <5% of the total number of viral infections. Respiratory syncytial virus was the most common coinfecting virus, and respiratory syncytial virus and influenza virus were the most common virus pair identified. In considering rapid diagnostic techniques, in 87% of the reports with available data a virus was diagnosed in >10% of specimens that were negative for the virus targeted by one method. There was no indication that mixed infections were associated with increased disease in immunocompetent patients or in certain immunocompromised patients. Immunocompromised patients, however, appeared to have a greater incidence of multiple infections. Mixed infections of single cells also occur and may have important clinical implications relative to reactivation of latent viruses and enhanced disease. The requirement for a comprehensive strategy for viral diagnosis involving multiple techniques was indicated by these findings.

Adhesion and Its Role in the Virulence of Enteropathogenic Escherichia coli. Derek Law

Summary: Enteropathogenic Escherichia coli (EPEC) organisms are an important cause of diarrheal disease in young children. The virulence of EPEC is a multifactorial process and involves a number of distinct stages. Initial adherence to intestinal mucosa is mediated by fimbriae which bring about a distinct form of adhesion, localized adhesion. Intimate adhesion of the bacterium to the eukaryotic membrane occurs, resulting in the activation of signal transduction pathways. Microvilli are disrupted and effaced from the apical membrane which then cups around the organism to form pedestal structures, the attaching and effacing lesion. Diarrhea may be produced by alteration of the permeability of the apical membrane and also through a malabsorption mechanism. The pathways involved in the production of the attaching and effacing lesion are described. EPEC organisms were originally thought to belong to a number of distinct serogroups; it is now apparent that many isolates belonging to these...
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serogroups are not pathogenic or belong to other pathogenic groups of E. coli. In addition, isolates falling outside of these serogroups are considered to be true EPEC. The definition of EPEC based on serotyping is inaccurate and should be replaced by methods that specifically detect the virulence properties of EPEC.

DNA Fingerprinting of Medically Important Microorganisms by Use of PCR. Alex van Belkum ................................. 174–184

Summary: Selected segments of any DNA molecule can be amplified exponentially by PCR. This technique provides a powerful tool to detect and identify minimal numbers of microorganisms. PCR is applicable both in diagnosis and in epidemiology. By amplification of hypervariable DNA domains, differences can be detected even among closely related strains. PCR fingerprinting is a valuable tool for medical microbiologists, epidemiologists, and microbial taxonomists. The current state of PCR-mediated genotyping is reviewed, and a comparison with conventional molecular typing methods is included. Because of its speed and versatility, PCR fingerprinting will play an important role in microbial genetics, epidemiology, and systematics.

Rationale for Cost-Effective Laboratory Medicine. Ann Robinson..... 185–199

Summary: There is virtually universal consensus that the health care system in the United States is too expensive and that costs need to be limited. Similar to health care costs in general, clinical laboratory expenditures have increased rapidly as a result of increased utilization and inflationary trends within the national economy. Economic constraints require that a compromise be reached between individual welfare and limited societal resources. Public pressure and changing health care needs have precipitated both subtle and radical laboratory changes to more effectively use allocated resources. Responsibility for excessive laboratory use can be assigned primarily to the following four groups: practicing physicians, physicians in training, patients, and the clinical laboratory. The strategies to contain escalating health care costs have ranged from individualized physician education programs to government intervention. Laboratories have responded to the fiscal restraints imposed by prospective payment systems by attempting to reduce operational costs without adversely impacting quality. Although cost containment directed at misutilization and overutilization of existing services has conserved resources, to date, an effective cost control mechanism has yet to be identified and successfully implemented on a grand enough scale to significantly impact health care expenditures in the United States.


Summary: The mammalian response to stress involves the release of soluble products from the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis. Cells of the immune system respond to many of the hormones, neurotransmitters, and neuropeptides through specific receptors. The function of the immune system is critical in the mammalian response to infectious disease. A growing body of evidence identifies stress as a cofactor in infectious disease susceptibility and outcomes. It has been suggested that effects of stress on the immune system may mediate the relationship between stress and infectious disease. This article reviews recent psychoneuroimmunology literature exploring the effects of stress on the pathogenesis of, and immune response to, infectious disease in mammals.


Summary: The nocardiae are bacteria belonging to the aerobic actinomycetes. They are an important part of the normal soil microflora worldwide. The type species, Nocardia asteroides, and N. brasiliensis, N. farcinica, N. oitidiscaviarum, N. nova, and N. transvalensis cause a
variety of diseases in both normal and immunocompromised humans and animals. The mechanisms of pathogenesis are complex, not fully understood, and include the capacity to evade or neutralize the myriad microbicidal activities of the host. The relative virulence of N. asteroides correlates with the ability to inhibit phagosome-lysosome fusion in phagocytes; to neutralize phagosomal acidification; to detoxify the microbicidal products of oxidative metabolism; to modify phagocyte function; to grow within phagocytic cells; and to attach to, penetrate, and grow within host cells. Both activated macrophages and immunologically specific T lymphocytes constitute the major mechanisms for host resistance to nocardial infection, whereas B lymphocytes and humoral immunity do not appear to be as important in protecting the host. Thus, the nocardiae are facultative intracellular pathogens that can persist within the host, probably in a cryptic form (L-form), for life. Silent invasion of brain cells by some Nocardia strains can induce neurodegeneration in experimental animals; however, the role of nocardiae in neurodegenerative diseases in humans needs to be investigated.

**Biology of Parainfluenza Viruses.** Raija Vainionpää and Timo Hyypia

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**Summary:** Parainfluenza virus types 1 to 4 (PIV1 to PIV4) are important human pathogens that cause upper and lower respiratory tract infections, especially in infants and children. PIV1, PIV2, and PIV3 are second only to respiratory syncytial virus as a cause of croup in young children. Although some clinical symptoms are typical of PIVs, etiologic diagnosis always requires detection of infectious virus, viral components, or an antibody response. PIVs are typical paramyxoviruses, causing a syncytial cytopathic effect in cell cultures; virus growth can be confirmed either by hemadsorption or by using immunological reagents. Currently, PIV is most often diagnosed by demonstrating viral antigens in clinical specimens by rapid and highly sensitive immunoassays. More recently, PCR has been used for the detection of PIVs. Serological diagnosis is made by detecting a rising titer of immunoglobulin G or by demonstrating immunoglobulin M antibodies. PIVs infect species other than humans, and animal models are used to study the pathogenesis of PIV infections and to test candidate vaccines. Accumulating knowledge on the molecular structure and mechanisms of replication of PIVs has accelerated research on prevention and treatment. Several strategies for vaccine development, such as the use of live attenuated, inactivated, recombinant, and subunit vaccines, have been investigated, and it may become possible to prevent PIV infections in the near future.