**Mycobacterium avium in the Postgenomic Era.** Christine Y. Turenne, Richard Wallace, Jr., and Marcel A. Behr .............. 205–229

Summary: The past several years have witnessed an upsurge of genomic data pertaining to the *Mycobacterium avium* complex (MAC). Despite clear advances, problems with the detection of MAC persist, spanning the tests that can be used, samples required for their validation, and the use of appropriate nomenclature. Additionally, the amount of genomic variability documented to date greatly outstrips the functional understanding of epidemiologically different subsets of the organism. In this review, we discuss how postgenomic insights into the MAC have helped to clarify the relationships between MAC organisms, highlighting the distinction between environmental and pathogenic subsets of *M. avium*. We discuss the availability of various genetic targets for accurate classification of organisms and how these results provide a framework for future studies of MAC variability. The results of postgenomic *M. avium* study provide optimism that a functional understanding of these organisms will soon emerge, with genomically defined subsets that are epidemiologically distinct and possess different survival mechanisms for their various niches. Although the status quo has largely been to study different *M. avium* subsets in isolation, it is expected that attention to the similarities and differences between *M. avium* organisms will provide greater insight into their fundamental differences, including their propensity to cause disease.

**Human Protothecosis.** Cornelia Lass-Flörl and Astrid Mayr ........ 230–242

Summary: Human protothecosis is a rare infection caused by members of the genus *Prototheca*. *Prototheca* species are generally considered to be achlorophyllic algae and are ubiquitous in nature. The occurrence of protothecosis can be local or disseminated and acute or chronic, with the latter being more common. Diseases have been classified as (i) cutaneous lesions, (ii) olecranon bursitis, or (iii) disseminated or systemic manifestations. Infections can occur in both immunocompetent and immunosuppressed patients, although more severe and disseminated infections tend to occur in immunocompromised individuals. *Prototheca wickerhamii* and *Prototheca zopfii* have been associated with human disease. Usually, treatment involves medical and surgical approaches; treatment failure is not uncommon. Antifungals such as ketoconazole, itraconazole, fluconazole, and amphotericin B are the most commonly used drugs to date. Among them, amphotericin B displays the best activity against *Prototheca* spp. Diagnosis is largely made upon detection of characteristic structures observed on histopathologic examination of tissue.

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**Avian Influenza Virus (H5N1): a Threat to Human Health.**  
J. S. Malik Peiris, Menno D. de Jong, and Yi Guan 243–267

Summary: Pandemic influenza virus has its origins in avian influenza viruses. The highly pathogenic avian influenza virus subtype H5N1 is already panzootic in poultry, with attendant economic consequences. It continues to cross species barriers to infect humans and other mammals, often with fatal outcomes. Therefore, H5N1 virus has rightly received attention as a potential pandemic threat. However, it is noted that the pandemics of 1957 and 1968 did not arise from highly pathogenic influenza viruses, and the next pandemic may well arise from a low-pathogenicity virus. The rationale for particular concern about an H5N1 pandemic is not its inevitability but its potential severity. An H5N1 pandemic is an event of low probability but one of high human health impact and poses a predicament for public health. Here, we review the ecology and evolution of highly pathogenic avian influenza H5N1 viruses, assess the pandemic risk, and address aspects of human H5N1 disease in relation to its epidemiology, clinical presentation, pathogenesis, diagnosis, and management.

**Problems in Diagnosing Scabies, a Global Disease in Human and Animal Populations.**  
Shelley F. Walton and Bart J. Currie 268–279

Summary: Scabies is a worldwide disease and a major public health problem in many developing countries, related primarily to poverty and overcrowding. In remote Aboriginal communities in northern Australia, prevalences of up to 50% among children have been described, despite the availability of effective chemotherapy. Sarcoptic mange is also an important veterinary disease engendering significant morbidity and mortality in wild, domestic, and farmed animals. Scabies is caused by the ectoparasitic mite Sarcoptes scabiei burrowing into the host epidermis. Clinical symptoms include intensely itchy lesions that often are a precursor to secondary bacterial pyoderma, septicemia, and, in humans, poststreptococcal glomerulonephritis. Although diagnosed scabies cases can be successfully treated, the rash of the primary infestation takes 4 to 6 weeks to develop, and thus, transmission to others often occurs prior to therapy. In humans, the symptoms of scabies infestations can mimic other dermatological skin diseases, and traditional tests to diagnose scabies are less than 50% accurate. To aid early identification of disease and thus treatment, a simple, cheap, sensitive, and specific test for routine diagnosis of active scabies is essential. Recent developments leading to the expression and purification of S. scabiei recombinant antigens have identified a number of molecules with diagnostic potential, and current studies include the investigation and assessment of the accuracy of these recombinant proteins in identifying antibodies in individuals with active scabies and in differentiating those with past exposure. Early identification of disease will enable selective treatment of those affected, reduce transmission and the requirement for mass treatment, limit the potential for escalating mite resistance, and provide another means of controlling scabies in populations in areas of endemicity.

**Helicobacter pylori Detection and Antimicrobial Susceptibility Testing.**  
Francis Mégraud and Philippe Lehours 280–322

Summary: The discovery of Helicobacter pylori in 1982 was the starting point of a revolution concerning the concepts and management of gastroduodenal diseases. It is now well accepted that the most common stomach disease, peptic ulcer disease, is an infectious disease, and all consensus conferences agree that the causative agent, H. pylori, must be treated with antibiotics. Furthermore, the concept emerged that this bacterium could be the trigger of various malignant diseases of the stomach, and it is now a model for chronic bacterial infections causing cancer. Most of the many different techniques involved in diagnosis of H. pylori infection are performed in clinical microbiology laboratories. The aim of this article is to review the current status of these methods and their application, highlighting the important progress which has been made in the past decade. Both invasive and noninvasive techniques will be reviewed.
Epidemiology and Control of Neosporosis and *Neospora caninum*.  

Summary: *Neospora caninum* is a protozoan parasite of animals. Until 1988, it was misidentified as *Toxoplasma gondii*. Since its first recognition in dogs in 1984 and the description of the new genus and species *Neospora caninum* in 1988, neosporosis has emerged as a serious disease of cattle and dogs worldwide. Abortions and neonatal mortality are a major problem in livestock operations, and neosporosis is a major cause of abortion in cattle. Although antibodies to *N. caninum* have been reported, the parasite has not been detected in human tissues. Thus, the zoonotic potential is uncertain. This review is focused mainly on the epidemiology and control of neosporosis in cattle, but worldwide seroprevalences of *N. caninum* in animals and humans are tabulated. The role of wildlife in the life cycle of *N. caninum* and strategies for the control of neosporosis in cattle are discussed.

Antimicrobial Resistance in *Haemophilus influenzae*.  
Stephen Tristram, Michael Jacobs, and Peter Appelbaum.

Summary: *Haemophilus influenzae* is a major community-acquired pathogen causing significant morbidity and mortality worldwide. Meningitis and bacteremia due to type b strains occur in areas where the protein-conjugated type b vaccine is not in use, whereas nontypeable strains are major causes of otitis media, sinusitis, acute exacerbations of chronic bronchitis, and pneumonia. Antibiotic resistance in this organism is more diverse and widespread than is commonly appreciated. Intrinsic efflux resistance mechanisms limit the activity of the macrolides, azalides, and ketolides. β-Lactamase production is highly prevalent worldwide and is associated with resistance to ampicillin and amoxicillin. Strains with alterations in penicillin binding proteins, particularly PBP3 (β-lactamase negative ampicillin resistant and β-lactamase positive amoxicillin-clavulanate resistant), are increasing in prevalence, particularly in Japan, with increasing resistance to ampicillin, amoxicillin, amoxicillin-clavulanate, and many cephalosporins, limiting the efficacy of expanded-spectrum cephalosporins against meningitis and of many oral cephalosporins against other diseases. Most strains remain susceptible to the carbapenems, which are not affected by penicillin binding protein changes, and the quinolones. The activity of many oral agents is limited by pharmacokinetics achieved with administration by this route, and the susceptibility of isolates based on pharmacokinetic and pharmacodynamic parameters is reviewed.