Multiresistant pathogens: The case of non-fermentative Gram-negative bacilli

Changes in classification of glucose-non-fermenting gram-negative bacilli

A. Bauernfeind. Max von Pettenkofer-Institut, München, Germany

Modern taxonomy is polyphasic and incorporates genotypic, phenotypic and phylogenetic markers. Genotypic characteristics are based on analysis of DNA or RNA molecules. rRNA is currently regarded as the optimal target for phylogenetic analysis as it is composed of highly conserved as well as variable domains. At this time direct DNA-sequencing of coding regions for 16S or 23S rRNA is widely performed. Phenotypic procedures include all non-nucleic acid directed approaches, e.g. composition of cell wall or cellular fatty acids, whole cell protein analysis etc.

Recent progress in technology allowed accumulation of new data leading to revisions in taxonomy and nomenclature (Bruckner & Colonna, CID, 1995) in major groups of bacteria. This holds true as well for glucose-non-fermenting gram-negative bacilli, e.g. Acinetobacter, Pseudomonas and others. Major reclassifications concern the genus Pseudomonas. It was subdivided into five rRNA-DNA-homology groups by Palleroni et al. in 1973. The genus Pseudomonas is now restricted to the former rRNA-group I, the species of rRNA-group II were transferred to the new genera Burkholderia and Ralstonia, rRNA-group III became the family Comamonadaceae, rRNA-group IV was transferred to the genus Brucella, and rRNA-group V to Xanthomonas.

Recently molecular procedures based on specific signature sequences within the 16S or 23S rRNA have been developed to identify species, e.g. within the genus Burkholderia. They improve identification of species difficult to separate by phenotypic procedures. There are, however, examples which demonstrate the limitations of genetic procedures, e.g. to differentiate between the phenotypically distinct species Burkholderia cepacia and B. vietnamiensis. This underlines the importance of polyphasic taxonomy for valid classification and nomenclature.

Cross-infection with Multiresistant Pseudomonas, Burkholderia and Other Non-Fermenters in Cystic Fibrosis Patients


The major Gram-negative pathogens responsible for respiratory infection and mortality in cystic fibrosis (CF) are Pseudomonas aeruginosa and Burkholderia cepacia. However, Stenotrophomonas maltophilia and Alcaligenes xylosoxidans and a few other non-fermenting species are emerging as possibly important pathogens due to the increased survival of the patients. All these species are increasingly resistant to most of the available antibiotics which are used extensively in CF patients. Difficult-to-treat strains and multiply resistant strains are therefore becoming an increasing problem in CF centres. Unfortunately, cross-infection has been documented with at least P. aeruginosa and B. cepacia in CF centres, in the wards, in the out-patient clinics, in summer-camps and during social activities such as fitness-classes. Even spread of epidemic strains between centres and between countries and between continents has been observed. Such transmissible strains are often multiply resistant due to the selective pressure imposed by the extensive use of antibiotics in CF patients. The most effective preventive measure has been the use of cohort isolation technique and high level of hygiene in CF centres and during social activities. The cohorting is based on bacteriological examination of sputum, and e.g. patients culture-positive for P. aeruginosa are kept isolated by geography and/or time from culture-negative patients. Social activities such as summer camps are completely avoided in some countries.

Acinetobacter: facts and fears

FD. Daschner. Institute for Environmental Medicine and Hospital Epidemiology, University Hospital, Freiburg, Germany

The presentation will cover the following facts: Epidemiological significance of cutaneous, pharyngeal and digestive tract colonisation by Acinetobacter, survival of Acinetobacter on dry surfaces, nosocomial outbreaks, risk factors for nosocomial colonisation, laboratory investigations of outbreaks, antimicrobial susceptibility.

Fears: Are hospital epidemiologists very much afraid of Acinetobacter? Why is it difficult to get rid of these organisms in hospitals? Are we colonising patients especially in intensive care units? Is there airborne spread of Acinetobacter?

Moraxella and Oligella: Ecology and Pathogenicity

A. von Graevenitz. CH

No abstract available.

Gene therapy: Where do we stand?

Retroviruses for Gene Delivery


We have demonstrated that the sensitivity of retroviruses to human serum is controlled by the expression of alpha 1-3 galactosyl sugar epitopes. We have now made high titer packaging cells producing viruses resistant to human serum. We are also attempting to retarget retroviruses to novel surface receptors using an insertion point in the MLV envelope which allows incorporation of an additional receptor binding domain. Our results with chimeric envelopes expressing ligands or single chain antibodies will be discussed. Finally, our strategies using retroviruses for tumour gene therapy will be presented. These include ex vivo modification of tumour cells which are being used in a melonoma vaccine clinical trial and targeting retroviral delivery to tumour cells.

Genetic Approaches for HIV Infection: Promises and Hurdles

D. Trono. Salk Institute for Biological Studies, San Diego, CA, USA

First developed for hereditary disorders, gene therapy is also envisioned for the treatment of oncologic and infectious diseases. In the latter case, gene modification of cells is aimed at reducing or ablating the replication of a pathogen, resulting in what has been called an "intracellular immunization". In spite of the recent success of pharmaceutical approaches for the management of HIV-induced disease, currently available antiviral drugs are toxic, costly, and need to be administered for an extremely long time, if not for the patients' entire life. Based on this premise, genetic approaches might represent a valid if only complementary approach for the treatment of HIV infection. The progress made towards meeting this objective, as well as the problems still remaining and their potential solutions, will be discussed.
Gene Therapy for Cystic Fibrosis: Where Do We Stand

E.W. E. Alton, Ion Transport Unit, National Heart & Lung Institute, London, United Kingdom

The cystic fibrosis (CF) gene was cloned was in 1989, and the feasibility of in vivo gene therapy demonstrated by 1991. With the development of CF mouse models, two groups demonstrated that CFTR gene transfer is able to correct, at least in part, the bioelectrical abnormality characteristic of CF. A result of these and other studies, CF gene transfer has moved into the clinical arena. Currently, 4 clinical trials have been reported with at least another dozen underway or recently completed. The preliminary data available from these studies suggests that both adenoviral and cationic liposome mediated gene transfer can be demonstrated at the level of both mRNA and protein. With respect to functional correction, approximately 30% of subjects studied have demonstrated evidence of some degree of correction of the chloride abnormality characteristic of CF. A number of safety issues have arisen with regard to adenoviral mediated gene transfer, whilst to date liposomes have proved to be safe. The data from these studies will be reviewed in this presentation.

Congenital Immuno-Deficiency

C. Bordignon

No abstract available.

Molecular Mediators of Brain Injury in Experimental Meningitis

M.G. Täuber, CH

No abstract available.

Latest Lessons from Experimental Models

M.G. Bergeron, Laval University, Québec City, Canada

Objectives: Animal models have been traditionally used to evaluate the pathogenesis of infectious diseases or to investigate the safety, pharmacokinetics, pharmacodynamics and/or efficacy of antimicrobials. From these models, parameters of antibiotic use have evolved and have helped in the management of specific diseases like meningitis or endocarditis. Recently some antibiotics have been shown to modulate host response. Appropriately designed, experimental models may become powerful tools to explore not only the in vivo antimicrobial activity of antibiotics but their Biological Response Modifiers (BRM) properties.

Methods: A murine model of pneumococcal pneumonia was developed i) to study the chronology of events which mediates the progression of the inflammatory response and leads to death, ii) to detect specific markers of disease progression, and iii) to evaluate how antibiotics can interact with the immune system and control this local infection.

Results: There was no correlation between the kinetics of cytokines in blood and that observed in bronchoalveolar fluid (BAL) or lung. The simultaneous elevation of IL-6 and TNF observed in blood may be a sign of poor prognosis and imminent death, while high level of IL-6 may suggest early disease with limited lung damage. In this model, cefotaxime (Ce) did reduce the level of LTB4 and neutrophil recruitment in the lungs of infected animals. Moreover, this β-lactam did selectively inhibit TNF and IL-6 in BAL and lung tissue without altering IL-1 production. By reducing the overwhelming inflammatory response that occurs during severe pneumonia, this antibiotic may protect the host in unique ways.

Conclusions: Animal studies based on developing strategies of immune modulation may eventually lead to therapies of unparalleled efficacy and safety.

Understanding Host Defence Mechanisms by Gene Manipulation

J.Y. Cesbron

No abstract available.

Pneumonia: News from the Experimental Models

W.R. Wilson, USA

No abstract available.

Evolving natural history and prognostic factors in febrile neutropenia


Since December 1994, the Infectious Committee of the Multinational Association for Supportive Care in Cancer (MASCC) is conducting a survey, in a multicentric, multinational setting among febrile neutropenic cancer patients (pts) in order to identify features at presentation able to predict a good outcome or the occurrence of a serious medical complication with a particular interest in an external validation of the prediction rule published by Talcott in JCO (1992) where pts are allocated into 4 groups: I: inpts, II: outpts with comorbidity, III: outpts with uncontrolled cancer, IV: outpts without comorbidity or uncontrolled cancer. Up to January 31, 1997, about 900 eligible pts have been followed for one episode. Interim descriptive results currently available are the following: median age is 52 yrs with 49% of male pts. Underlying disease was hematologic in 46%, lymphoma/Hodgkin's disease in 20%, solid tumor in 26% and other in 9%. 23% did undergo a transplantation. A clinical site was found in 42% and Talcott's group distribution was: I:62%, II:13%, III:9% and IV:16%. Initial empiric antibiotic treatment was successful in 55%, a serious medical complication occurred in 17% with a 7% death rate. Closure of the survey will occur soon, after 1000 episodes and definitive results including inferential analysis will be available at the meeting.