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Selected projects

Investigation of *Stenotrophomonas maltophilia* by Multi Locus Sequence Typing

Stenotrophomonas maltophilia is an ubiquitous environmental species, which is also found as an opportunistic pathogen colonising or infecting especially immunocompromised patients. Previously 10 different genogroups have been delineated on the base of Amplified Fragment length Polymorphism (AFLP) [Hauben et al. 1999]. To obtain more information about the genetic population structure we are developing a Multi Locus Sequence Typing (MLST) scheme for this species, utilizing seven housekeeping genes. Seventy strains from all over the world are analysed including type strains, representatives of the 10 AFLP genogroups and subsequent isolates from 5 hospital outbreaks. Among the 70 *S. maltophilia* isolates 54 STs and 38 to 53 alleles for the single loci could be observed. We could confirm 9 of 10 genogroups and identified five new groups. Three genogroups each included exclusively ST from isolates of either clinical or environmental origin. Twelve out of 19 isolates from epidemiologically non-associated cystic fibrosis patients clustered in one particular genogroup. Considering all isolates a significant "Index of Association" indicated to a "linkage disequilibrium" as expected for clonal species. Accordingly, the Pearson-correlation and the „likelihood score“- tests demonstrated a good congruence for the single loci-trees except for two loci. On the other Hand, there was evidence for intragenic recombination as detected by the maximum chi-squared test. The unusual separation from isolates of different ecological origins into distinct genogroups requires further investigations.

Finished projects

Genodiversity of Resistant *Pseudomonas aeruginosa* in Relation to Antimicrobial Usage and Resistance Rates in Intensive Care Units

The objective of this study was to prove the assumption that resistance rates in intensive care units (ICUs) are markedly influenced by cross-transmission events, beside high antimicrobial usage.

This was a prospective ICU and laboratory-based surveillance study involving 35 German ICUs from 1999 through 2004. Five hundred and eighty-five ciprofloxacin or imipenem-resistant isolates of *Pseudomonas aeruginosa* were investigated, together with resistance rates (RR) and unit-based antimicrobial use (AD). Antimicrobial use was reported in terms of defined daily doses (DDDs) per 1,000 patient-days. All the strains were assigned to ICU-based genotypes. Genodiversity was calculated as the numbers of indistinguishable ICU-based genotypes found per isolates tested. Reduced ICU-based genodiversity was taken as an indirect measure of frequently occurring cross-transmission events.

The genodiversity of ciprofloxacin as well as imipenem-resistant *P. aeruginosa* isolates was significantly lower (Fisher $P < 0.05$) in ICUs with high RR and low AD (0.50 and 0.50) than in those ICUs that featured low RR in the presence of high AD (0.90 and 0.95). In ICUs with low genodiversity, there was a stronger rise of RR with increasing AD than in ICUs with high diversity.

This study on resistant *P. aeruginosa* supports the assumption that high RR in the presence of low AD results from more frequent cross-transmission events. A stronger rise of RR with increasing AD in ICUs with a low genodiversity indicates that RR in ICUs might be markedly determined by cross-transmission events beside antimicrobial usage.

Plasmid-mediated quinolone-resistance (qnr) in German ICUs

The occurrence of a novel plasmid-mediated quinolone resistance has been reported in a few cases outside Europe. This transmissible quinolone resistance gene (qnr) was detected in isolates from patients in the USA, China and Egypt. Molecular analysis demonstrated the location of the qnr-gene in class I integrons. The aim of this study was to determine the prevalence of qnr-positive strains in German ICUs.

Six hundred and forty-eight fluoroquinolone or cephalosporin-resistant Enterobacteriaceae and *Acinetobacter* spp., obtained from 34 ICUs during the last three years were screened for the presence of integrons. One hundred and thirty-four strains containing integron cassettes as well as integrase sequences were tested for the presence of the qnr gene-locus by use of PCR.

One isolate of *Enterobacter* spp. from a German ICU patient turned out to be qnr-positive as well as five *Citrobacter freundii* strains from three patients treated in a South-German ICU during a one month period. All *C. freundii* strains were indistinguishable by use of XbaI macrorestriction analysis. Moreover, none of these quinolone-resistant strains were susceptible to cefoxitin, ceftazidime or cefotaxime.

This is one of the first reports of qnr-positive strains obtained from patients in Europe. Molecular epidemiology suggests that qnr-positive strains were involved in an outbreak in one ICU. The spread of transmissible quinolone-resistance might be underscored.