# Department of Infection Control

Seiji Hori, *Professor*
Hiroshi Takeda, *Assistant Professor*
Tetsuya Horino, *Assistant Professor*
Masaki Yoshida, *Associate Professor*
Yasushi Nakazawa, *Assistant Professor*

## General Summary

We performed clinical research on urinary tract infection and bacteremia caused by extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli*, *Streptococcus* sp., and methicillin-sensitive *Staphylococcus aureus* (MSSA) as bacterial infections. Our results suggest methods for the appropriate diagnosis and treatment of these infectious diseases to all physicians. In addition, we showed the efficacy of nontechnical skills for infection control that suggested a new strategy independent of any equipment. We will extend these investigations to basic research and large prospective studies.

## Research Activities

*Prevalence and drug susceptibilities of ESBL-producing E. coli strains isolated from urine*

We investigated the prevalence and drug susceptibilities of ESBL-producing *E. coli* isolated from urine and the genotyping of ESBL to clarify strategies against urinary tract infections caused by these bacteria. From March 2010 through June 2012 ESBL-producing *E. coli* were isolated from 41 patients in The Jikei University Katsushika Medical Center. Their median age was 76 years. Nineteen patients (46.3%) had community-acquired infections. Forty-one strains of ESBL-producing *E. coli* were detected. The minimal inhibitory concentrations of 17 antimicrobials — latamoxef, flomoxef, cefmetazole, imipenem, meropenem, doripenem, faropenem, sulbactam/ampicillin, clavulanic acid/amoxicillin, tazobactam/piperacillin, sulbactam/cefoperazone, levofloxacin, ciprofloxacin, sitafloxacin, gentamicin, amikacin, and tobramycin — against these strains were measured with the broth microdilution method according to the Clinical and Laboratory Standards Institute. In addition, genotyping of ESBLs was performed with the polymerase chain reaction. Results of genotyping of ESBLs were as follows: the CTX-M-9 group, 31 strains (75.6%); the CTX-M-1 group, 6 (14.6%); and the CTX-M-2 group, 4 (9.8%). All strains were sensitive to meropenem, doripenem, imipenem, tazobactam/piperacillin, latamoxef, flomoxef, cefmetazole, faropenem, and amikacin, and 73% of these strains were sensitive to sitafloxacin. However, 73.2% of these strains were levofloxacin-resistant. These results indicate that ESBL-producing *E. coli* are frequently resistant to levofloxacin. Therefore, in the future we should pay attention to the choice of antimicrobials for urinary tract infections caused by ESBL-producing *E. coli* and continuously examine their drug susceptibilities.

*Teaching nontechnical skills is effective for infection control*

We used TeamSTEPPS (Team Strategies and Tools to Enhance Performance and Patient

Safety), a popular educational tool for nontechnical skills, to teach infection-control compliance to healthcare workers in The Jikei University Hospital in 2013. In particular, "cross-monitoring and feedback" were applied to develop hand-hygiene compliance in each hospital unit. After these efforts, the total consumption of alcohol hand rub showed a 29.6% increase from the previous year. The teamwork tools of TeamSTEPPS are useful for developing infection-control compliance in the hospital.

*Predictive factors for metastatic infection in patients with bacteremia caused by MSSA*
Metastatic infections, such as infective endocarditis and psoas abscess, are serious complications of *S. aureus* bacteremia, because failure to identify these infections may result in bacteremia relapse or a poor prognosis. In the present study, we determined predictive factors for metastatic infection due to MSSA bacteremia. A retrospective cohort study was performed among patients with MSSA bacteremia at The Jikei University Hospital from January 2008 through December 2012. Factors analyzed included the underlying disease, initial antimicrobial treatment, and primary site of infection. During the 5-year study period, 73 patients met the inclusion criteria and were assessed. The most common primary site of bacteremia was catheter-related bloodstream infection (25 of 73 patients [34.2%]). Metastatic infection occurred in 14 of 73 patients (19.2%) (infective endocarditis, 3 patients; septic pulmonary abscess, 3 patients; spondylitis, 4 patients; psoas abscess, 4 patients; epidural abscess, 3 patients; and septic arthritis, 1 patient). Six patients had multiple metastatic infections. Multivariate analysis revealed that the predictive factors associated with the development of metastatic infection were a delay in appropriate antimicrobial treatment of > 48 hours, persistent fever for > 72 hours after starting antibiotic treatment, and lowest C-reactive protein levels of > 3 mg/dL in the 2 weeks after the onset of bacteremia. This study demonstrated that additional diagnostic tests should be performed to identify metastatic infection, particularly in patients with delayed antimicrobial treatment, persistent fever, and persistently high C-reactive protein levels.

*Analysis of the components of the biofilm formed by clinical strains of staphylococci*
The components of the biofilm formed by staphylococci are polysaccharides, proteins, and extracellular DNA. These biofilms are thought to be composed of components in complexes or alone. In the biofilm formation assay, staphylococci formed a biofilm rich in polysaccharides with the addition of 4% NaCl to brain heart infusion broth. This is presumably due to the high osmotic pressure in the medium. The pH of the medium was lowered with the addition of 1% glucose, and proteins were the main components of the biofilm. By means of this phenomenon, clinically isolated staphylococci were divided into non-biofilm-forming strains, polysaccharide biofilm-forming strains, and proteinaceous biofilm-forming strains. In the biofilm destruction assay, we tested a variety of enzymes to destroy the biofilms formed by staphylococci. Proteinase K destroyed the proteinaceous biofilms, and polysaccharide biofilm were susceptible to dispersin B. On the other hand, the susceptibilities to DNase were nonidentical in clinical isolates.

*Acquired immunodeficiency syndrome and malignancy*

Although infection with the human immunodeficiency virus (HIV) has become a controllable chronic illness because of improvements in antiretroviral agents, complications not related to acquired immunodeficiency syndrome (AIDS), such as cardiovascular diseases, dementia, and malignancy, have become major problems. Of these complications, malignancy is an important and critical issue.

Malignancies in patients with HIV were classified into 2 types: AIDS-defining malignancies (ADMs) and non-AIDS-defining malignancies (NADMs). Recently, NADMs are more frequent than ADMs, the management of NADMs matters currently. The most common NADMs are Hodgkin lymphoma, lung cancer, cervical/anal cancer, and hepatocellular carcinoma.

The clinical course of malignancy in patients with HIV is generally aggressive, and most cases are difficult to treat. However, early diagnosis and radical surgical resection improve the prognosis. Therefore, we must be concerned about primary and secondary prevention of malignancy as well as the treatment of AIDS. Primary prevention measures that should be implemented include the control of co-infection by oncogenic viruses, the avoidance of exposure to environmental oncogenic factors, and the earlier start of antiviral therapy. As a secondary prevention measure, medical checkups similar to those for patients without HIV are recommended for all patients with HIV.

In our hospital, we treated a patient with AIDS who had invasive thymoma and another patient who had penile cancer, the surgical treatment of which resulted in cure without relapse. Early diagnosis and treatment of malignancy might contribute to good outcomes in patients with HIV.

## Publications

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