# Department of Infection Control

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## General Summary

We demonstrated the morbidity of asymptomatic sexually transmitted infections in patients with human immunodeficiency virus (HIV) infection and of metastatic infections during *Staphylococcus aureus* bacteremia. These results suggest the necessity of an active approach for identifying latent infectious diseases. In addition, we showed the validity of new antibiotic treatments for extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and of preventive medicine for malaria. Thus, our investigations suggest new strategies to diagnose, treat, and prevent infectious diseases.

## Research Activities

*Asymptomatic sexually transmitted infections in HIV-infected patients*
We performed a questionnaire survey about sexual behavior and a survey about urethra-pharyngeal *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections in outpatients infected with HIV but without symptoms of urethritis or pharyngitis. Specimens of pharyngeal gargle (10 ml of saline) and urine were examined for *C. trachomatis* and *N. gonorrhoeae* with the strand displacement amplification method. We measured antibodies (immunoglobulins A and G) against *C. trachomatis*. We performed a survey of sexual behavior in 77 patients (mean age, 40.1 years). Although *C. trachomatis* was detected in the urine of only 1 patient, antibodies against *C. trachomatis* were detected in 46 of the 77 patients (59.7%).

*Analysis of atovaquone-proguanil compared with mefloquine in the chemoprophylaxis of malaria in nonimmune Japanese travelers*
Malaria is a severe, extremely common infectious disease in tropical and subtropical areas. For high-risk travelers to endemic regions, malaria chemoprophylaxis is recommended. Internationally, atovaquone-proguanil, mefloquine, or doxycycline is prescribed for malaria chemoprophylaxis. However, in 2012 atovaquone-proguanil and doxycycline were not approved for use in Japan. Therefore, the data on atovaquone-proguanil for malaria chemoprophylaxis in Japanese travelers are not clear. We analyzed data from a questionnaire survey to assess the safety and tolerability of atovaquone-proguanil and compare them with those of mefloquine for nonimmune Japanese travelers. Atovaquone-proguanil was given to 278 travelers and mefloquine to 38 travelers. The mean duration of each prophylaxis was 20.0 ± 9.6 days for atovaquone-proguanil and mefloquine for 59.0 ± 15.9 days. Nine travelers discontinued treatment (5 with atovaquone-proguanil and 4 with mefloquine), and the rate of discontinuation was significantly less with atovaquone-proguanil. The frequency of adverse events was sig-

nificantly less with atovaquone-proguanil (18.8%, 52 cases) than with mefloquine group (36.8%, 14 cases). In particular, the frequency of psychoneurotic adverse events was significantly less with atovaquone-proguanil. These results suggest that atovaquone-proguanil is better tolerated and produces fewer adverse events than mefloquine in non-immune Japanese travelers.

*Drug susceptibilities of ESBL-producing* Escherichia coli *strains isolated from urine*
We investigated the drug susceptibilities of ESBL-producing *E. coli* isolated from urine and performed genotyping of ESBLs. The genotypes of the ESBLs were the CTX-M-9 group in 75.6%, the CTX-M-1 group in 14.6%, and the CTX-M-2 group in 9.8%. All strains were sensitive to meropenem, doripenem, imipenem, flomoxef, latamoxef, sitafloxacin, cefmetazole, tazobactam/piperacillin, and amikacin. Ninety percent of the strains were sensitive to faropenem. However, 73.2% of the strains were resistant to levofloxacin. There was no relationship between drug susceptibility and the genotype of ESBLs. Antimicrobial agents should be carefully selected for the treatment of urinary tract infections caused by ESBL-producing *E. coli*.

*Predictive factors for metastatic infection in patients with bacteremia caused by* Staphylococcus aureus
Metastatic infections, such as infective endocarditis and psoas abscess, are severe complications of *S. aureus* bacteremia, because failure to identify metastatic infections may lead to relapsing bacteremia or poor outcomes. To determine predictive factors for metastatic infection of *S. aureus* bacteremia, we analyzed several factors, including the underlying disease, initial antimicrobial treatment, and primary site of infection. From January 2008 through December 2011, 40 patients met the inclusion criteria of this study. Of the cases of bacteremia in these patients, 33 were caused by methicillin-sensitive *S. aureus*. Metastatic infection occurred in 11 (27.5%) of the 40 patients. The predictive factors associated with the development of metastatic infection identified with multivariate analysis were unknown primary site of infection and fever persisting for more than 72 hours after the start of antibiotic treatment.

*The capacity to form biofilms and the biofilm component of staphylococci*
Staphylococci are able to attach to abiotic or biotic surfaces and form biofilms, which lead to chronic infections. We analyzed the capacity to form biofilms and the biofilm component *in vitro* of clinically isolated staphylococci. Biofilm formation in brain-heart infusion broth was similarly observed in 48 strains of *S. aureus* (29%) and 28 strains of *Staphylococcus epidermidis* (25%). One biofilm formed by *S. aureus* and 4 biofilms formed by *S. epidermidis* were susceptible to polysacacharide degradative enzyme (dispersin B). These results indicate that the biofilms formed by *S. epidermidis* contain more polysaccharide than do biofilms formed by *S. aureus*.

*Clinical analysis of the immunological background of patients with nontuberculous mycobacteriosis*
We are investigating the pathophysiology of infections in patients with nontuberculous

mycobacteriosis and correlating immunological variables with images of bronchopulmonary lesions.

## Publications

***Yoshida M, Hoshina T, Tamura K, Kawano S, Kato T, Sato F, Nakazawa Y, Yoshikawa K, Onodera S, Hori S.*** An HIV patient with hepatic flare after the initiation of HBV-active antiretroviral therapy. *Intern Med.* 2012; **51:** 1623-6.

***Yoshida M, Chiba A, Kawano S, Kato T, Sato F, Horino T, Nakazawa Y, Yoshikawa K, Onodera S, Hori S.*** Comparison of free and anonymous testing for HIV and sexually transmitted infections between the University Hospital and Health Center. *J Infect Chemother.* 2012; **18:** 704-8.

***Nakazawa Y, Ii R, Tamura T, Hoshina T, Tamura K, Kawano S, Kato T, Sato F, Horino T, Yoshida M, Hori S, Sanui M, Ishii Y, Tateda K.*** A case of NDM-1-producing *Acinetobacter baumannii* transferred from India to Japan. *J Infect Chemother.* 2013; **19:** 330-2. Epub 2012 Sep 12.

***Onodera S, Onoe Y, Hosobe T, Kato T, Yoshida M.*** Efficacy and safety of levofloxacin to non-gonorrheal urethritis (in Japanese). *Jpn J Antibiot.* 2012; **65:** 399-409.

***Kato T, Okuda J, Ide D, Amano K, Takei Y, Yamaguchi Y.*** Questionnaire-based analysis of atovaquone-proguanil compared with mefloquine in the chemoprophylaxis of malaria in non-immune Japanese travelers. *J Infect Chemother.* 2013; **19:** 20-3.

***Matsubara K, Yumiko H.*** Analysis of *Clostridium difficile* infection at a community hospital in Japan (in Japanese). *Nihon Rinsho Chonai Biseibutsu Gakkai Kaishi*. 2012; **14:** 63-8.

***Sato F, Chiba A, Kawano S, Kato T, Horino T, Hori S.*** Vertebral osteomyelitis due to biofilm producing *Staphylococcus epidermidis* (in Japanese). *BACTERIAL ADHERENCE & BIOFILM.* 2012; **25:** 75-8.

## Reviews and Books

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***Yoshida M.*** Emergence and control of a new multidrug resistant bacteria (in Japanese). *Nihon Naika Gakkai Zasshi.* 2012; **101:** 3134-42.

***Yoshida M.*** Antibiotics (in Japanese). *Karada no Kagaku.* 2013; **276:** 320-5.

***Nakazawa Y.*** The approach of management of HIV post exposure prophylaxis for health care workers (in Japanese). *INFECTION CONTROL.* 2012; **Suppl**: 126-32.

***Horino T, Yoshida M.*** Norovirus Infection (in Japanese). *Kagaku Ryoho no Ryoiki.* 2012; **28:** 2228-33.

***Horino T.*** Rapid diagnosis of urinary tract infection (in Japanese). *Shonika Rinsho.* 2012; **65:** 2477-82.

***Horino T.*** HIV infection (in Japanese). *Karada no Kagaku.* 2013; **276:** 68-72.

***Horino T.*** Sepsis due to gram negative bacteria (in Japanese). *Kansen to Kokinyaku.* 2013; **16:** 56-61.

***Sato F, Yoshida M.*** Needs of high dose antibiotics (in Japanese). *Kansen to Kokinyaku.* 2012; **15:** 320-5.

***Sato F.*** Malaria (in Japanese). *Karada no Kagaku.* 2013; **276:** 83-7.

***Kato T.*** Infections in splenectomised patients (in Japanese). *Rejidento Note.* 2012; Suppl ER Note **6**: 283-6.

***Hosaka Y, Yoshida M.*** Carbapenem (in Japanese). *Kansen to Kokinyaku.* 2012; **15:** 150-4.