

Department of Infection Control

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General Summary

We performed both basic and clinical research in the following areas: bacterial infection and chemotherapy, opportunistic infection in patients with human immunodeficiency virus/acquired immunodeficiency syndrome, and outbreak and infection control.

Research Activities

Analysis for pathogenic factors of methicillin-resistant Staphylococcus aureus isolated by a blood culture

In cases of bloodstream infection caused by *S. aureus*, severe metastatic infections, such as infective endocarditis, septic pulmonary embolism, and iliopsoas abscess, may occur and lead to a patient's death. This trend is more common in methicillin-resistant *S. aureus* (MRSA) bacteremia than in methicillin-sensitive *S. aureus* (MSSA) bacteremia. Previously we revealed that in MSSA bacteremia, predictive factors for 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 for 2 weeks after the onset of bacteremia. To analyze the predictive factors for metastatic infection due to MRSA bacteremia, we performed a broth microdilution method for the antibiotic susceptibility testing of 23 isolates that were clinically isolated during 2013. All 23 isolates were susceptible to vancomycin, teicoplanin, linezolid, daptomycin, and arbekacin according to the Clinical Laboratory and Standards Institute criteria, which indicated that the appropriate antibiotics were selected. We are now investigating the host-related predictive factors and MRSA-related pathogenic factors.

Clinical studies of combination antimicrobial therapy against multidrug-resistant Pseudomonas aeruginosa with the Break-point Checkerboard Plate method

We studied the effects of combination antibiotic therapy with the Break-point Checkerboard Plate method against clinical isolates obtained at our hospital from 33 cases of multiple-drug resistant *P. aeruginosa* bacteremia. Two combination therapies — colistin plus aztreonam, and amikacin plus aztreonam — showed synergistic effects. Two cases of multiple-drug resistant *P. aeruginosa* bacteremia were successfully treated with the combination antimicrobial therapy of amikacin plus aztreonam.

Meta-analysis of urinary tract infections in patients receiving a sodium-dependent glucose co-transporter 2 inhibitor

The aim of this meta-analysis study was to determine the relationship between sodium-dependent glucose co-transporter 2 (SGLT2) inhibitors and urinary tract infections in

patients with diabetes mellitus. Of 27 studies reviewed, only 9 showed that patients receiving an SGLT2 inhibitor had an increased rate of urinary tract infections. On the other hand, none of these studies showed an increased rate of severe renal infections, such as pyelonephritis or urosepsis. In addition, in many studies that evaluated the efficacy of SGLT2 inhibitors, the definition, classification, and additional risk factors of urinary tract infections were not described.

Revisiting a method for diagnosing toxoplasmosis: Development of the Toxoplasma Killing Observation test

Toxoplasma gondii, the most successful protozoan, infects approximately one-third of persons worldwide. In most people who are infected, except for pregnant women and immunocompromised patients, toxoplasmosis is a self-limited disease with mild symptoms or no symptoms. Immunocompromised patients, such as those who have acquired immunodeficiency syndrome, have undergone organ transplantation, or use steroids, are at risk for *Toxoplasma* encephalitis, pneumonitis, and retinitis. Most of these cases are caused by relapses and flares from the bradyzoite, a slowly duplicating form of *Toxoplasma* which is dormant in host tissues. On the other hand, primary infection during pregnancy is a risk factor for congenital toxoplasmosis, which causes intrauterine growth retardation, hydrocephaly, mental growth retardation, retinitis, and even fetal death.

Many types of serodiagnosis are widely used to detect toxoplasmosis around the world. However, because immunoglobulin (Ig) G and IgM are the only antibodies against *Toxoplasma* available for serodiagnosis in Japan, diagnosis can be complicated. If toxoplasmosis has relapsed in patients, IgM is usually negative, and even if IgG is positive the present infection cannot be discriminated from previous infections. The diagnosis of congenital toxoplasmosis with IgG and IgM is another issue. Some studies have found that IgM remains over the threshold for more than 2 years and that the positive predictive value of IgM is only 45.98%. This kinetics of IgM has a risk of leading to misdiagnosis.

The Sabin-Feldman dye test has been used since 1948. The dye test uses the serum of a subject to evaluate the aggregate ability of a tachyzoite-cidal immunoglobulin titer. The classic serodiagnosis test still has high sensitivity and specificity as confirmed diagnosis. A problem with the dye test is the complicated evaluation method, in which stained tachyzoites must be counted under visual recognition. We examined this problem with a tachyzoite expressing green fluorescent protein, which is an alternative marker for evaluating the deactivation of the tachyzoite. The new, improved dye test, the *Toxoplasma* Killing Observation test, has the advantages of objectivity and retention for evaluation and provides outcomes equivalent to those of the classic Sabin-Feldman dye test.

Effect of infection control team round against Gram-negative bacilli bacteremia at Kashiwa Hospital

At Kashiwa Hospital, the infection control team (ICT) makes rounds for patients with positive blood cultures and has an intervention for the proper use of antibiotics. We examined the effects of the ICT's rounds against Gram-negative rod (GNR) bacteremia in the hospital. In the 6 months from August 31 to March 1, 2015, we investigated the cases in which GNR had been detected in blood cultures. After drug-susceptibility testing, the

attending physician changed the antibiotic to one with a narrow-range spectrum (de-escalation) in about half of the patients with GNR bacteremia. De-escalation could be promoted by the ICT rounds. After ICT intervention, the use of antibiotics was appropriate. In the future, cooperation is needed between the ICT and attending physicians.

Drug-resistant bacteria have become a major social problem

We performed a questionnaire without filling in the hospital name in 750 Japanese teaching hospitals to investigate the present conditions of infection control in Japan. The status of basic infection control measures, such as the hand hygiene and antimicrobial stewardship, was included in the questionnaire. We received answers from 369 hospitals (49.2%). Questions about MRSA isolation in 2013 were answered by 286 hospitals and produced a mean isolation rate of 46.8%. Questions about the consumption of alcoholic hand disinfectant by an entire ward, except the operating room, were answered in 2013 by 248 hospitals, leading to a median consumption rate of 6.0 ml/patient-day. Therefore, in Japan, the basic infection control measures should be quickly improved. Especially needed is the improvement of hand hygiene.

Publications

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