

## Department of Infection Control

---

Seiji Hori, *Professor*  
Hiroki Tsukada, *Professor*  
Yasushi Nakazawa, *Associate Professor*  
Hiroshi Takeda, *Assistant Professor*

Masaki Yoshida, *Professor*  
Koji Yoshikawa, *Associate Professor*  
Tetsuya Horino, *Associate Professor*

### General Summary

This year we investigated the seroprevalence of *Toxoplasma gondii* among patients with human immunodeficiency virus (HIV) infection and the rate of enterocolitis when HIV infection is diagnosed. These studies will contribute to the early diagnosis and appropriate treatment of HIV infection. In addition, we demonstrated the safety and tolerability of medicinal *Trichuris suis* ova (TSO), a result that should accelerate further studies of new strategy for inflammatory bowel diseases.

### Research Activities

*Safety and tolerability of medicinal TSO in healthy Japanese volunteers: a randomized, double-blind, placebo-controlled trial*

Background: Medicinal use of TSO, and its potential for improving the immunomodulatory capacity of the human immune system, has been verified in several studies. To the best of our knowledge, earlier research has been limited to only European and American subjects, among which Asian subjects are poorly documented. Therefore, we performed a clinical trial to reveal the safety and tolerability of TSO therapy among the Japanese population.

Methods: The study was a randomized, double-blind, placebo-controlled trial held at The Jikei University Hospital. Twelve subjects were stratified into 3 TSO dose-dependent groups (TSO 1,000, 2,500, and 7,500), and 1 subject in each group was randomly assigned to the control group. Subjects were limited to healthy Japanese men aged at least 20 years. Single doses of medicinal TSO or placebo were given, and all subjects were followed up for 56 days after ingestion. During the follow-up period, clinical practitioners checked each subject at the clinic at postingestion days (PIDs) 7, 14, 28, and 56. Subjects were asked of clinical symptoms with a questionnaire-based self-report, which was filled out at every visit. Blood samples were drawn at PIDs 7, 14, 28, and 56. Stool samples were collected at PIDs 28 and 56.

Results: During the study period, no severe adverse events occurred in any subject. However, during the observational period participants in each TSO group had mild to moderate abdominal symptoms: diarrhea, bloating, and appetite loss. One subject in the placebo group had mild diarrhea. Stool samples were fully collected, and microscopic examinations detected no TSO in samples. Blood samples showed raised eosinophil count in several subjects, especially in the groups with a higher dose of TSO. No extra-abdominal symptoms developed in any subject.

Conclusions: All doses of TSO were well tolerated, without severe adverse events. On the

other hand, mild to moderate abdominal symptoms developed in several subjects. We believe that medicinal use of TSO would be safe for Japan, but detailed follow-up is recommended for sustainable usage.

*Seroprevalence and associated factors of Toxoplasma gondii among HIV-infected patients in Tokyo: A cross sectional study*

An HIV infection, particularly in patients in whom acquired immunodeficiency syndrome (AIDS) has developed, carries a risk of toxoplasmosis with encephalitis, which is mostly caused by a form (bradyzoite) of the protozoan parasite *Toxoplasma gondii*. HIV/AIDS in Japan has been recognized as a serious health issue in recent years. In this study, to elucidate *T. gondii* seroprevalence in HIV-positive patients in Japan and associated characteristics with *Toxoplasma* parasite infection, the titer of *T. gondii* immunoglobulin (Ig) G (Tg-IgG) was measured in 399 HIV-positive patients who visited a hospital in Tokyo from 2015 through 2017. A questionnaire survey was also conducted to investigate associations of lifestyle and customs. The overall prevalence of Tg-IgG-positive serum was 8.27% (33 of 399 subjects). Positivity for Tg-IgG was confirmed with the Sabin-Feldman dye test; the titers between each examination with strongly correlated ( $p < 0.001$ ,  $r = 0.6$ ). The *T. gondii* infection rate was found to be correlated with age ( $p < 0.001$ ) but was not significantly correlated with lifestyle customs, such as consuming undercooked meat and having a pet cat. An association was observed between *T. gondii* infection and the experience of living in Hokkaido ( $p = 0.001$ ). These results suggest that the rate of previous exposure to *T. gondii* parasites is similar among HIV-positive and HIV-negative populations in Japan and provides clear information about the potential risk of *T. gondii* encephalitis.

*Enterocolitis in the patients with HIV infection*

The clinical course of HIV infection is divided into acute HIV infection, clinical latency, and AIDS. Because the most common symptom of acute HIV infection is fever, following lymphadenopathy, throat pain, and skin eruption, physicians should consider HIV infection when patients have infectious mononucleosis, measles, or rubella. In addition, 30% of HIV patients have diarrhea as a symptom in the acute infection phase. Immunosuppression and microbial dysbiosis in the intestine due to HIV infection cause diarrhea in patients in the acute phase of HIV infection. In this study, we investigated the reason HIV infection was diagnosed in The Jikei University Hospital. We found that HIV infection was diagnosed in 30 of 667 patients when they had diarrhea or bloody stool. In these patients, the most common pathogens were *Entamoeba histolytica*, in 11 patients, and cytomegalovirus, in 5 patients. *Cryptosporidium* infection, salmonellosis, giardia intestinalis, *Campylobacter* infection were each diagnosed in 1 patient. These results suggest that physician should notice digestive symptom in HIV patients and consider HIV infection in patients with enterocolitis.

## Publications

Hoshina T, Horino T, Saiki E, Aonuma H, Sawaki K, Miyajima M, Lee K, Nakaharai K, Shimizu A,

**Hosaka Y, Kato T, Sato F, Nakazawa Y, Yoshikawa K, Yoshida M, Hori S, Kanuka H.** Seroprevalence and associated factors of *Toxoplasma gondii* among HIV-infected patients in Tokyo: A cross sectional study. *J Infect Chemother.* 2020 Jan; **26**(1): 33-37. doi: 10.1016/j.jiac.2019.06.012. Epub 2019 Jul 23. PubMed PMID: 31350182.

**Hoshina T, Fukumoto S, Aonuma H, Saiki E, Hori S, Kanuka H.** Seroprevalence of *Toxoplasma gondii* in wild sika deer in Japan. *Parasitol Int.* 2019 Aug; **71**: 76-79. doi: 10.1016/j.parint.2019.03.016. Epub 2019 Mar 30. PubMed PMID: 30940609.

**Kuroda Y, Taguchi K, Enoki Y, Matsumoto K, Hori S, Kizu J.** Age-Associated Theophylline Metabolic Activity Corresponds to the Ratio of 1,3-Dimethyluric Acid to Theophylline in Mice. *Biol Pharm Bull.* 2019; **42**(8): 1423-1427. doi: 10.1248/bpb.b19-00232. PubMed PMID: 31366878.

**Saida Y, Watanabe S, Abe T, Shoji S, Nozaki K, Ichikawa K, Kondo R, Koyama K, Miura S, Tanaka H, Okajima M, Terada M, Ishida T, Tsukada H, Makino M, Iwashima A, Sato K, Matsumoto N, Yoshizawa H, Kikuchi T.** Efficacy of EGFR-TKIs with or without upfront brain radiotherapy for EGFR-mutant NSCLC patients with central nervous system metastases. *Thorac Cancer.* 2019 Nov; **10**(11): 2106-2116. doi: 10.1111/1759-7714.13189. Epub 2019 Sep 10. PubMed PMID: 31507098; PubMed Central PMCID: PMC6825912.

**Yanagihara K, Matsumoto T, Aoki N, Sato J, Wakamura T, Kiyota H, Tateda K, Hanaki H, Ohsaki Y, Fujiuchi S, Takahashi M, Akiba Y, Masunaga S, Takeuchi K, Takeda H, Miki M, Kumagai T, Takahashi H, Utagawa M, Nishiya H, Kawakami S, Ishigaki S, Kobayashi N, Takasaki J, Mezaki K, Iwata S, Katouno Y, Inose R, Niki Y, Kawana A, Fujikura Y, Kudo M, Hirano T, Yamamoto M, Miyazawa N, Tsukada H, Aso S, Yamamoto Y, Iinuma Y, Mikamo H, Yamagishi Y, Nakamura A, Ohashi M, Kawabata A, Sugaki Y, Seki M, Hamaguchi S, Toyokawa M, Takeya H, Fujikawa Y, Mitsuno N, Ukimura A, Miyara T, Hayashi M, Mikasa K, Kasahara K, Koizumi A, Korohashi N, Matsumoto T, Yosimura Y, Katanami Y, Takesue Y, Wada Y, Sugimoto K, Yamamoto T, Kuwabara M, Doi M, Simizu S, Tokuyasu H, Hino S, Negayama K, Mukae H, Kawanami T, Yatera K, Fujita M, Kadota J, Hiramatsu K, Aoki Y, Magarifuchi H, Oho M, Morinaga Y, Suga M, Muranaka H, Fujita J, Higa F, Tateyama M.** Nationwide surveillance of bacterial respiratory pathogens conducted by the surveillance committee of Japanese Society of Chemotherapy, the Japanese Association for Infectious Diseases, and the Japanese Society for clinical microbiology in 2014: General view of the pathogens' antibacterial susceptibility. *J Infect Chemother.* 2019 Sep; **25**(9): 657-668. doi: 10.1016/j.jiac.2019.05.006. Epub 2019 Jun 10. PubMed PMID: 31196772.

**Watanabe N, Saito K, Kiritani A, Fujimoto S, Yamanaka Y, Fujisaki I, Hosoda C, Miyagawa H, Seki Y, Kinoshita A, Takeda H, Endo Y, Kuwano K.** A case of invasive pulmonary aspergillosis diagnosed by transbronchial lung biopsy during treatment for diabetic ketoacidosis in a type 1 diabetic patient. *J Infect Chemother.* 2020 Feb; **26**(2): 274-278. doi: 10.1016/j.jiac.2019.08.011. Epub 2019 Sep 19. PubMed PMID: 31542205.

**Izumisawa T, Kaneko T, Soma M, Imai M, Wakui N, Hasegawa H, Horino T, Takahashi N.** Augmented Renal Clearance of Vancomycin in Hematologic Malignancy Patients. *Biol Pharm Bull.* 2019 Dec 1; **42**(12): 2089-2094. doi: 10.1248/bpb.b19-00652. Epub 2019 Sep 18. PubMed PMID: 31534058.

## Reviews and Books

**Horino T, Hori S.** Metastatic infection during *Staphylococcus aureus* bacteremia. *J Infect Chemother.* 2020 Feb; **26**(2): 162-169. doi: 10.1016/j.jiac.2019.10.003. Epub 2019 Oct 30. Review. PubMed PMID: 31676266.