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Editorial Note

More attention to the field

Kenji Hirayama, M.D., Ph.D.
Editor-in-Chief
Tropical Medicine and Health

Japanese Developments in 2005-2006

In 2005, the Institute of Tropical Medicine of Nagasaki University (located in Nagasaki, Japan) received two significant governmental grants for the establishment of field-based laboratories in Nairobi, Kenya and Hanoi, Vietnam. At the same time, the Research Institute for Microbial Diseases of Osaka University, Institute of Medical Science of the University of Tokyo and Research Center for Zoonosis Control of Hokkaido University received similar grants for the establishment of overseas laboratories in Bangkok, Thailand and Beijing, China. Thus, 2005 was a watershed year for Japan and affiliated countries in initiating long-term research projects aimed at the control of regional as well as global infectious diseases, such as TB, AIDS, malaria, influenza, dengue fever as well as other emerging and neglected or unknown diseases.

Figure 1 shows the proposed network of research groups newly organized by these grants from the Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan.

Other independent activities supported by the Ministry of Health, Welfare and Labour (MOHL) and the Ministry of Agriculture and Fishery (MOAF) have been launched to control domestic and imported microbe infections in humans and animals. All of these activities are organized by the cabinet office of the government.

Global Issues

One important reason for the Japanese government recognition of infectious disease control as a high-priority issue stems of course from the endemicity of serious emerging infectious diseases such as HIV, TB, BSE, West Nile fever, SARS, and avian influenza and the threat they pose to Japanese citizens.

But another reason may be even more compelling. That is the surprisingly small number of experts and researchers working in this scientific field in Japan. The grave shortage of human resources is a problem not only for Japan but for all the developed countries, including the United States and European countries where public health priorities tend to concentrate in areas such cancer, hypertension, ischemic heart disease and diabetes.

In the past five to ten years, therefore, the fact that developed countries are more concerned than ever about the possible endemicity of new and old infectious diseases has been reflected in the G8 summit meetings held in the U.S. A., Japan and the U.K. During those meetings, malaria, TB, and HIV/AIDS were recognized as three major diseases confronting the international community. Now tropical medicine and international health researchers are expected to contribute more to solve the problems underlying the endemicity of these infectious diseases.

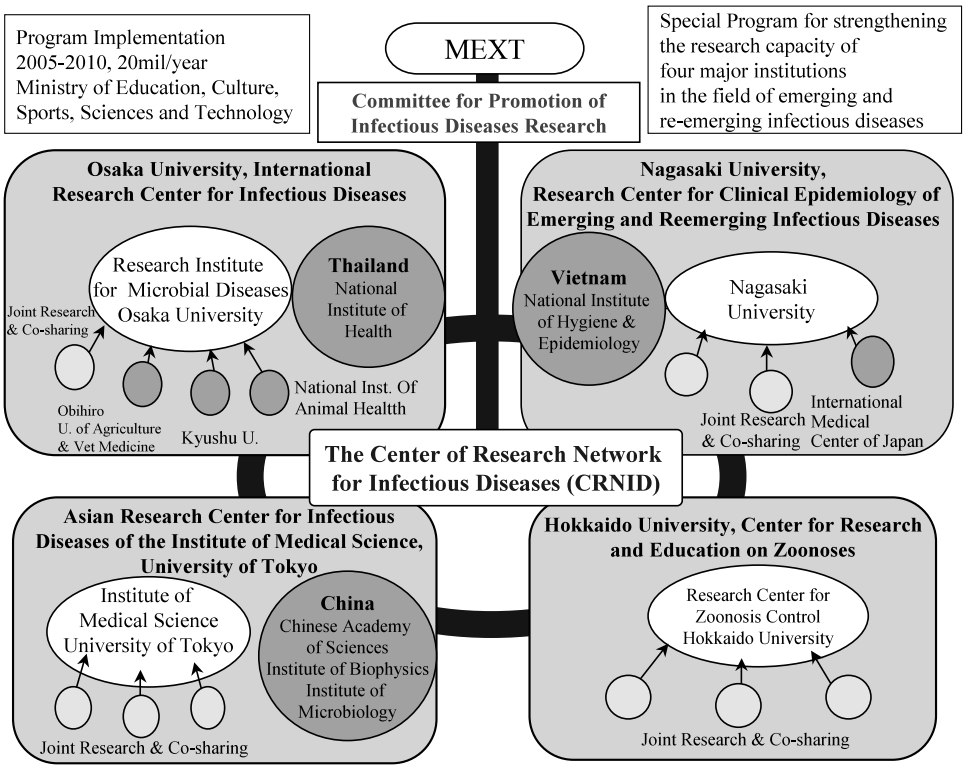

Figure 1

The Responsibility of Researchers

Generally speaking, research is a personal and private undertaking, and the quality of its outcome is almost totally dependent on individual ability, capacity and the work environment. Without competent personnel, good research cannot be performed, but, recently, the environment of research activities is gaining greater attention.

The word “environment” includes different conditions surrounding researchers, as shown in Figure 2. The following four points are all important aspects of environment:

1. Life lines such as professional position, salary, housing, and insurance.
2. Hardware such as academic institution, university, laboratory, bench, equipment, reagents and of course money.
3. Research team members such as post doctoral fellows, associates and assistants, students, technicians, sponsors, and administrative officers.
4. Software such as motivation, information, peer review and evaluation systems, and the place of discussions.

Each researcher bears responsibility to manage all the related business shown above. Scientific journals, meanwhile, have an important role in the category of software.

Editorial Policy of “Tropical Medicine and Health”

Peer review and swift publication are our priorities. All the editorial staff members endeavor to accomplish this policy.

1. Original papers are published preferably according to the following criteria:
   1) Endemic field-based, originated, oriented or implicated study.
   2) Scientifically and ethically sound study.
   3) Not only positive results but also negative, where noteworthy.
   4) Concise, clear and definitive but not over-simplified.
   5) Modest, humble and appropriate discussion.
2. Review papers are welcome without invitation.
   1) Review must be short and clear enough to deliver the important and relevant messages and/or information using figures and illustrations.
   2) Scientific meeting report by our special correspondent will be published for relevant meetings such as our annual meeting, WHO/TDR, UNICEF, JICA, NIH meeting, international symposia, workshops and conferences held by Asian, African, American and European societies.
   3) Special issues will be added by the editors.
3. Discussion and Information
   1) Letter to the editor
   2) Opportunity for funding and positions
   3) Society Calendar
   4) Other relevant information

Personal Goal

When everyone concerned agrees that “Tropical Medicine and Health” is a readable, enjoyable, reliable and stimulating journal, I will bid farewell to my editorial desk. I hope that this will be within the next five years. Your kind cooperation is essential for this accomplishment.

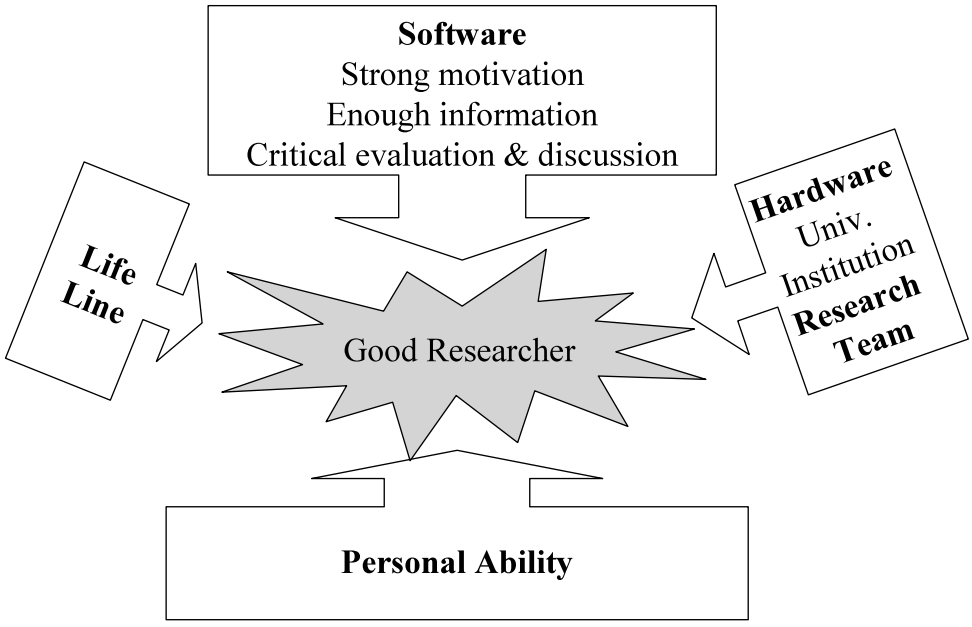

Figure 2

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EPIDEMIOLOGICAL STUDY OF INFLUENZA VIRUS INFECTIONS IN YANGON, MYANMAR

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Accepted 14, December, 2005

Abstract: Although influenza is a highly contagious acute respiratory illness of global importance, little is known about the disease in tropical countries. An influenza survey was conducted in three sentinel sites in Yangon, Myanmar from September 2003 to December 2004. Throat or nasal swabs were collected from 616 patients with influenza-like symptoms and tested using rapid diagnostic test kits and virus isolation. Influenza B virus was detected in 6 patients from September to October, 2003. Influenza A viruses were detected in 133 patients from June to September, 2004, and the 51 influenza A viruses isolated from 72 specimens were all A/H3N2. Influenza virus infections occurred mainly in the rainy season in Yangon, Myanmar, but continuous ongoing influenza surveillance is needed.

Key words: influenza, acute respiratory infection, rapid diagnostic test kit, Yangon

INTRODUCTION

Influenza epidemiology varies according to the geographical location and climate. Influenza occurs mainly during winter in the temperate zones [1-3]. However, little is known about the epidemiology and seasonality of influenza in tropical zones, where influenza virus infections occur throughout the year with either no distinct seasonality or relatively intense activity during the rainy season [4-12].

Myanmar is divided into three areas; upper (northern), central, and lower (southern) Myanmar. The central and southern areas belong to the tropical zone while the northern area belongs to the temperate zone. The average temperature is 25℃ to 33℃ in the cold and rainy season (May-September or October), and 32℃ to 43℃ in the dry season (November-April). The rainfall ranges from 500 mm in the central dry zone to 5,000 mm in the coastal regions. Yangon, the capital city of Myanmar, has a tropical monsoon climate.

No epidemiological study of influenza virus infections has been conducted in Myanmar to date. We conducted the first study in Yangon from September 2003 to December 2004 and clarified the seasonality of influenza virus infections.

MATERIALS AND METHODS

Survey on Influenza Virus Infections in Yangon, Myanmar

The respiratory chest unit and pediatric department at Sanpya Hospital in Yangon were selected as sentinel sites for the study from September 2003 to December 2004. Two general practitioners working in the central Yangon also joined the study from June 2004.

The patients with influenza-like symptoms who participated in this study presented with a combination of symptoms such as fever of more than 38℃, coughing, rhinorrhea, myalgia, arthralgia, and diarrhea. A standardized questionnaire was used to obtain demographic data, medical history, and clinical features for each patient.

Virus Antigen Detection and Virus Isolation

Throat or nasal swabs were collected at the first clinic visit and subjected to influenza A and B virus antigen detection using influenza diagnostic kits (QUICK-S INFLU A/B "SEIKEN", Denka Seiken Co. Ltd, Tokyo, Japan). The positive specimens were placed in viral transport media, and then aliquoted in cryotubes and kept at −80℃ in freezers at Sanpya Hospital for further laboratory examinations.

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Specimens were transferred in frozen conditions and tested in the Department of Public Health, Niigata University Graduate School of Medical and Dental Sciences. Specimens were centrifuged at a low-speed and the supernatants inoculated into Madin Darby Canine Kidney (MDCK) cells to observe cytopathic effect (CPE) for influenza viruses. Type and subtype were determined by hemagglutinin inhibition (HI) tests with type- and subtype-specific antisera against 2004/05 influenza vaccine strains, such as A/New Caledonia/20/99 (H1N1), A/Wyoming/3/2003 (H3N2), and B/Shanghai/361/2002 (Denka Seiken Co. Ltd., Tokyo, Japan).

RESULTS

A total of 616 patients were tested with rapid diagnostic test kits during the study period, and none had a history of influenza vaccination. In 90% of patients, throat or nasal swabs were collected within the first 3 days after the onset of symptoms.

Among the 616 patients, influenza B viruses were detected in 6 patients (1%) in September and October 2003, all under 14 years of age. Influenza A viruses were detected in 133 patients (21.6%) from June to October with a peak in June 2004 **(Fig 1)**. The majority were under 14 years of age (88.7%), and only two patients were over 60 years of age **(Table 1)**. The sex ratio was 1.42 (men/female).

The clinical symptoms of influenza-positive patients did not differ from those of influenza-negative patients **(Table 2)**. The clinical diagnosis of patients with influenza-like symptoms was influenza, bronchiolitis, pneumonia, tuberculosis, respiratory syncytial virus infection, dengue fever, or enteritis.

A total of 72 specimens from the 616 patients tested with rapid tests were available for further virological examinations, and influenza viruses were isolated from 51 specimens (70.8%). All of these isolated strains were antigenically similar to A/Wyoming/3/2003 (H3N2), but not to A/New Caledonia/20/99 (H1N1) or B/Shanghai/361/2002.

Fig. 1. Number of influenza test positive patients per week, 2003-2004

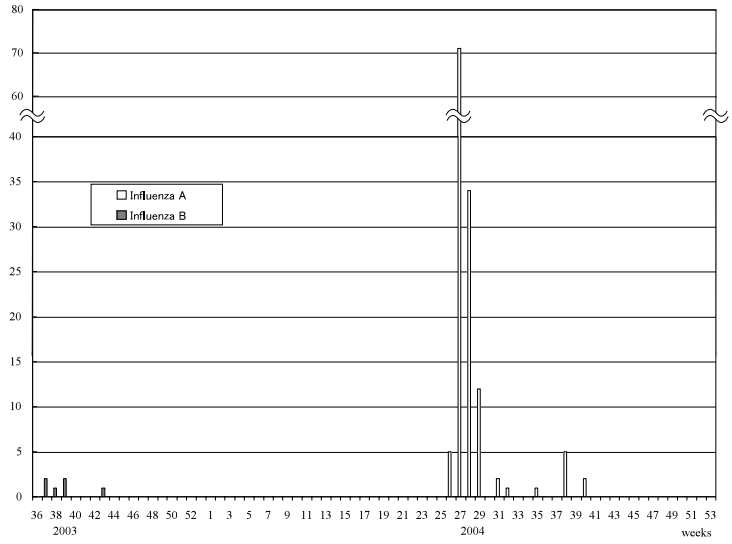

Table 1. Age distribution and percentage of influenza patients.

age	type A	type B	negative	total	% (positive)
0-4	79 (59.4)	2 (33.3)	324 (67.9)	405 (65.7)	20.0%
5-9	33 (24.8)	3 (50.0)	45 (9.4)	81 (13.1)	44.4%
10-14	6 (4.5)	1 (16.7)	18 (3.8)	25 (4.1)	28.0%
15-19	1 (0.8)	0	12 (2.5)	13 (2.1)	7.7%
20-59	12 (9.2)	0	64 (13.4)	76 (12.3)	15.8%
60-	2 (1.5)	0	10 (2.1)	12 (1.9)	16.7%
ND	0	0	4 (0.8)	4 (0.6)	0.0%
total	133 (100%)	6 (100%)	477 (100%)	616 (100%)	22.6%

ND: No data of age. Numbers in bracket are percentages.

Table 2. Clinical symptoms of influenza virus positive and negative cases

	Influenza viruses	
Clinical symptoms	Positive cases	Negative cases
fever (>38 ℃)	100%	100%
cough	95.5%	96.0%
rhinorrhea	97.0%	88.7%
myalgia	31.6%	28.0%
arthralgia	9.8%	16.1%
diarrhea	12.8%	16.9%

DISCUSSION

We conducted a sentinel surveillance of influenza virus infections in Yangon city from September 2003 to December 2004 and detected influenza B viruses at the end of the rainy season (Sept-Oct) in 2003 and influenza A viruses in the rainy season (June-Oct) in 2004.

Influenza virus infections are more common in winter in temperate countries but vary in tropical countries [6-12]. It has been noted that influenza viruses survive more readily in aerosols under conditions of low temperature and low humidity [13, 14]. These conditions coincide with the mechanism of seasonality of influenza in temperate countries, but the correlation is not clear in tropical countries. In tropical countries such as Thailand, Singapore and Indonesia, influenza viruses are detected throughout the year with one or two peaks depending on the study year, but there is not always a correlation between rainy seasons and peaks of influenza virus infections. In Singapore, no correlation has been found between influenza activity and climatic conditions or influx of travelers [10]. Mortality from influenza is probably greatly underestimated or not even reported in these regions because of the lack of good surveillance programs in many tropical countries. Our study in Yangon was a preliminary study of only one year in duration. Thus, further long-term studies in Yangon and other areas should be important additions to the epidemiology of influenza in tropical areas.

Between October 2003 and September 2004 in the neighboring country of Thailand, influenza B and A (H3) viruses co-circulated, the former predominating in 2003 and the latter in 2004 [4, 5]. Our study was insufficient in terms of subject number and study period, but the epidemiological data from these two countries was quite similar. In 2004, influenza A/H3N2 viruses predominated in Yangon as in many countries [4, 5]. Most of these isolated strains were antigenically similar to A/Wyoming/3/2003 (H3N2), a component of the 2004/2005 influenza vaccines recommended by WHO. They belonged to A/Fujian-like strain, which had circulated in Asia since 2002 and caused major epidemics worldwide in the 2003/2004 winter [4, 5]. Since virological surveillance is quite limited in tropical areas including Southeast Asian countries, the epidemiological study in Myanmar is important to global influenza surveillance. In our study, the rapid test-positive samples obtained in Myanmar were sent to Japan for virus isolation, and viruses were isolated from approximately 71% of the samples, suggesting that this manner of international collaborative study, though perhaps not ideal, is a viable option for participation in the WHO influenza surveillance network.

The clinical symptoms of influenza-positive patients did not differ significantly from those of influenza-negative patients in this study. The lack of differential diagnosis sometimes leads to misdiagnosis and the misuse of antibiotics. Therefore, the development and application of affordable test kits to detect pathogens other than influenza may also be helpful for the diagnosis of febrile diseases in tropical countries.

ACKNOWLEDGMENTS

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THE ROLE OF SOCIAL SCIENCE RESEARCH IN REDUCING THE BURDEN OF TUBERCULOSIS IN HIGH HIV PREVALENCE SETTINGS

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Accepted 23, January, 2006

Abstract: Tuberculosis (TB) is a global public health problem. The HIV/AIDS epidemic negatively affects tuberculosis control in many countries. The United Nations has set the Millennium Development Goals (MDGs) aiming to halve TB prevalence and mortality by the year 2015. In this paper, the authors summarize the global situation of TB associated with HIV/AIDS (TB/HIV), WHO's interim policy on TB/HIV, as well as the status and needs of social science research. The authors reviewed two major social interventions which are critical for TB control in HIV high prevalence settings, namely those to reduce stigma and those to promote adherence to TB/HIV medication. The review suggests that more social science research should be implemented in resource limited countries.

Key words: tuberculosis, HIV/AIDS, TB/HIV, social science research, social interventions

"The battle against AIDS will not be won unless the international community does more to fight TB as well".
Nelson Mandela, former president of South Africa and former tuberculosis patient
The 15th International AIDS Conference, Bangkok, Thailand, 15 July 2004

Why does fighting AIDS need to involve fighting TB?

HIV/AIDS and tuberculosis (TB) are the world's first and second leading causes of death from infectious diseases. If there had been no HIV epidemic, TB would have been controlled. In 2005, it is estimated that about 40.3 million adults and children were living with HIV and about 3.1 million have died from AIDS [1]. About8.8million new cases of TB occurred in 2003 with an estimated 1.7 million dying from the disease. In the same year, about 674,000 new cases of TB were associated with HIV (TB/HIV), and 229,000 people with HIV/AIDS (PHA) died from TB [2]. Tuberculosis is the leading cause of morbidity and mortality among PHA. At least one in three will develop TB [3]. The alarming global crisis of HIV/AIDS and TB has prompted the United Nations and the international community to set a global target to reduce these priority diseases. The Millennium Development Goals (MDGs) aim to reverse the incidence and halve the mortality of these two diseases by the year 2015 [4].

Biologically, it is well known that TB enhances HIV replication and accelerates HIV progression, thereby shortening the life expectancy of PHA [5]. The close interaction between TB and HIV/AIDS indicates the need to reduce the burden of both HIV/AIDS and TB. Most Sub-Saharan African countries with high HIV prevalence have suffered the negative impact of the interaction between HIV/AIDS and TB for more than a decade. WHO recently published the first interim policy on collaborative TB/HIV activities to tackle the dual epidemics [6]. Table 1 presents the WHO's recommended interventions to reduce the burden of TB and HIV/AIDS. The biomedical interventions to reduce TB and HIV burden include antiretroviral therapy (ARV) and cotrimoxazole preventive therapy (CPT) for HIV-positive TB patients and isoniazid (INH) to prevent TB among PHA. The results of clinical research show that CPT can prolong lives and ARV can reduce death among HIV-positive TB patients [7-10]. INH can reduce the risk of developing TB among PHA [11]. Despite the efficacy of these medical interventions, the task of reducing the TB/HIV burden in resource-limited settings is a great challenge and necessitates interventions suggested by social science research.

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[2]TB/HIV Research Foundation, Chiang Rai, Thailand.

Why social science research?

To control the epidemic of TB and HIV/AIDS, we must not only deal with the HIV virus and the TB bacteria but also manage patients who carry these germs and educate the health worker who deliver health services to the population. Human behavior and social environments are complicated, and biomedical interventions alone are not sufficient for disease control. It has consistently been proposed that TB and AIDS are social diseases whose patterns of transmission must be understood, not only through the clinical or laboratory studies of bacteria and virus, but also through the study of attitudes, behavior and social organization [12-19]. In particular, HIV/AIDS provides a tragic example of a complex interactions between the disease agent and human behavior, which further complicates the effort to control tuberculosis. How can social science research contribute to TB prevention and care in high HIV prevalence settings?

Based on the social science research in the northernmost province of Thailand where HIV epidemic fuels the TB epidemic (HIV prevalence among pregnant women was 3.7% and TB incidence was 140/100,000), we summarized the psycho-social interactions between HIV/AIDS and TB and the negative impact on TB and HIV/AIDS prevention and care (table 2) [20]. It is noteworthy that this social science research was carried out before ARV was available to the poor people of Thailand. Increased access to antiretroviral therapy among people with AIDS in Thailand and other resource-limited countries might reduce AIDS related fatalism and stigma [21, 22]. But even though several high HIV prevalence countries in sub-Saharan Africa successfully mobilized free ARV for poor patients, stigma and discrimination, especially among women resulted in a low level of participation in HIV testing and access to ARV. Gender inequality is such that a poor woman is placed in an even worse social situation if her husband or in-laws become aware of her HIV status [1]. These complicated circum-

Table 1: Interventions to reduce the burden of TB and HIV/AIDS recommended by the World Health Organization [6]

A. Interventions for collaboration between TB and AIDS programs
A.1. Set up a coordinating body for TB/HIV activities effective at all levels
A.2. Conduct surveillance of HIV prevalence among tuberculosis patients
A.3. Carry out joint TB/HIV planning
A.4. Conduct monitoring and evaluation
B. Interventions to decrease the burden of tuberculosis in people living with HIV/AIDS
B.1. Establish intensified tuberculosis case-finding
B.2. Introduce isoniazid preventive therapy
B.3. Ensure tuberculosis infection control in health care and congregate settings
C. Interventions to decrease the burden of HIV in tuberculosis patients
C.1. Provide HIV counseling and testing
C.2. Introduce HIV prevention methods
C.3. Introduce co-trimoxazole preventive therapy
C.4. Ensure HIV/AIDS care and support
C.5. Introduce antiretroviral therapy

Table 2: The psycho-social interactions between HIV/AIDS and TB and the negative impact on TB and HIV/AIDS prevention and care in Thailand (before a lunching the government's policy on access to ARV in 2003) [20, 22, 33-35]

Psycho-social interactions between HIV/AIDS and TB
● The social stigma attached to HIV/AIDS is enormous and results in denial of HIV testing and delay in access to TB and HIV care
● Serious AIDS stigma and an inadequate knowledge about TB symptoms results in delays in seeking TB care because TB symptoms are comparable to AIDS and people with TB symptoms were afraid of HIV/AIDS
● Most HIV negative TB patients were stigmatized as having AIDS.
● The high mortality among HIV-positive TB patients during TB treatment discredited the TB treatment efficacy. Health staff had a low motivation to care for the patients because the treatment results were so discouraging.
● Fatalism attached to HIV/AIDS hindered the patients access to health care patients felt hopeless and lacked the motivation to adhere to their TB treatment.

Table 3: List of some interventions to reduce TB and HIV/AIDS stigma and desired outcomes [36-40]

Interventions to reduce stigma	Desired outcomes
Mass communication interventions Television, radio, newspaper or poster presenting the followings: - photos and news of countries' leaders or popular persons telling about their experiences of having TB or HIV/AIDS; showing close embrace with patients; showing acceptance for HIV blood testing; showing TB is curable or showing that they are surviving from HIV/AIDS - photos and news of Miss HIV/AIDS stigma contest	- increase public's acceptance and reduce discrimination - promote early HIV testing - reduce delay in seeking care
Training/workshop -Intensive training course to reduce stigma among health workers -Community awareness-raising through participatory training -Involving HIV-positive long-term survivors in education and training	-improve health workers' attitude towards TB and AIDS patients and willingness to care for them. -increase HIV testing and access to care
Counseling -Individual or family counseling by health workers or by HIV-positive counselor	-reducing self-stigma; reduce anxiety and stress; disclosure HIV to spouse and family members
Social mobilization and community participation -Establishing network (self-help group) of PHA and motivate PHA to join the network -Financial assistance to PHA and family -Involving PHA, religion leaders and community leaders in policy making, and in the development and implementation of programs.	-reducing self-stigma -empowering PHA -increasing HIV testing and disclosure of HIV status
Improving health service system and promoting access to treatment -Free and effective treatment -Integrating HIV/AIDS care with other chronic diseases clinics -PHA-Friendly hospital	-increase access to HIV care -increase HIV testing -reduce discrimination feeling
Law and regulation intervention - Law or regulation against stigma in general - Law or regulation for the work places - Code of professional ethics/code of practice - Standard or universal guidelines	- protection of patients' right - patients are eligible for petition the court and receive support for complaint due to stigma.

Table 4 Scope of adherence to medication in TB/HIV care [41]

Scope of adherence to medication in TB/HIV care	Targeted HIV-positive person	Expected health outcome of good adherence	Potential negative impact of non-adherence
Adherence to TB preventive Therapy	HIV-infected persons with latent TB infection (no clinical TB symptoms)	- Reducing risk to become sick with TB	- drug resistance
Adherence to TB treatment	HIV- positive TB patients (having TB symptoms)	-cure from TB and do not transmit TB to others	-death -treatment failure -drug resistant -continue transmitting TB to others
Adherence to antiretroviral therapy (ARV)	AIDS patients (usually CD4 < 200cells/mm^3)	-prolong life, better quality of life -avoid opportunistic infection -reduce risk of HIV transmission	-drug resistant -treatment failure -death

Table 5 Interventions for improving adherence to medication [13, 20, 42-44].

Interventions for enhancing adherence to medication
Improving health service systems -Eliminating or lowering user fees -Providing directly observed therapy (DOT) -Organizing service hours convenient for patients and minimizing waiting time -Active follow-up system for non-adherent patients -Offering health education and counseling service by using linguistically and culturally appropriate messages. -Hospitalization may prevent non-adherence among patients exhibiting the profile of defaulter (e.g. homeless, alcoholic patients) -Involving people with HIV/AIDS network and community leaders in delivery services (e.g. providing medication education, follow up non-adherent cases, home visit)
Improving attitude and performance of health care providers -Good relationship between health providers and patients significantly improves patient adherence. -The providers should render service with courtesy and respect for patients. -The providers should understand patients' needs and constraints, understand patients' cultural differences in attitudes to disease. -The providers should spend more time listening to patients. -Giving rewards to health provider who achieve high adherence rate
Facilitating patient medication -Providing special packages of medicine such as a daypack for easier medication. -Prescribing medication once a day and fixing a time such as before breakfast or before bed. -Providing several medicine reminding system (alarm clock, calendar, reminding through pager or cell phone, linking medication time to daily life activity)
Providing incentives to patient and community -Providing transportation support to attend clinics, shelter support for homeless people, offering meals and assistance with job skills for poor patients -Giving rewards to patients who adhere well to the treatment. -Paying a deposit at the start of their treatment, which entitles the patient to cheaper drugs and is refundable on good adherence to prescribed course.

Table 6 Literature on social science research in TB in comparison with AIDS cited by the National Library of Medicine (NLB) website [26].

Searching keywords ..... AND TB ..... AND AIDS	TB (no. of papers)	AIDS (no. of papers)
Social sciences AND	1837	25,028
Behavioral research AND	4	515
Qualitative research AND	13	141
KAP AND (Knowledge, Attitude, Practice)	4	132
Poverty AND	137	1007
Stigma AND	31	433

Table 7 Study topics and geographic location of tuberculosis behavioral and social science research (n=175) [45]

Research settings	
-USA-based	47%
-International-based	36%
-Non-location specific (e.g. concept, position papers)	17%
Study topics	
-Patient adherence	47%
-Social, cultural factors (including Knowledge-Attitude-Belief)	45%
-Structural influences	33%
-Health seeking behavior	19%
-Provider adherence	14%
-Others	12%

stances require social science research to identify socially and culturally sensitive behavioral interventions.

UNAIDS and WHO identify stigma and adherence to medication as the major challenges in controlling the HIV/AIDS epidemic [1, 23]. In this article, we discuss two major social and behavioral interventions, namely interventions to reduce stigma (table 3) and interventions to promote adherence to TB/HIV medications (table 4, 5). These two social interventions are important prerequisites for implementing the medical interventions recommended by WHO (table 1). For example, interventions for reducing AIDS stigma can facilitate HIV testing for TB patients, and interventions for enhancing adherence are important to ensure treatment efficacy and to prevent drug resistance when patients receive ARV, CPT and INH.

Status of social science research in TB and TB/HIV

In 1975, the Special Program for Research and Training in Tropical Diseases (TDR), a globally coordinated effort of the United Nations Children's Fund (UNICEF), United Nations Development Program (UNDP), World Bank and World Health Organization (WHO), was established to combat neglected tropical diseases and diseases of the poor and disadvantaged [24]. In view of the importance of research in social sciences to control communicable diseases, TDR started supporting social science research in 1979. However, social science research for tuberculosis is still quite new to TDR, as shown by the fact that TDR added tuberculosis to the tropical disease portfolio only in 1999 [25]. Table 6 clearly shows that TB has received much less attention from social science researchers in comparison to HIV/AIDS. According to the United States National Library of Medicine (the world's largest literature database for medical and public health research), the number of TB social science research articles in scientific journals is 7 to 128 times less than HIV/AIDS articles [26]. Obviously, social science research in HIV/AIDS has received ample recognition because results of this research help to identify interventions to reduce the HIV/AIDS burden [27]. However, the role of social science research in improving TB care, especially in developing countries, is oddly limited for such an old disease as TB. A recent review of the 175 social science articles on TB (table 7) shows that half of the studies were conducted in the United State (Rawls and Booker, 2005), although 95 percent of global TB cases and99percent of TB deaths occur in the developing world [2]. Clearly, therefore, it is imperative that more social science research be conducted in high burden and resource-limited countries.

The difficulty of achieving the global target for TB control is mainly due to the lack of human resources and qualified staff [28]. At the global level, the published information on human resources and TB control are limited and almost none relate to HIV-TB control [29]. Training is essential to the development of a health workforce geared to TB control, but regular international TB training courses are organized by a limited number of organizations [30, 31]. Most international training courses focus on clinical or laboratory training and the management of tuberculosis programs. To our knowledge, none of these courses include social science subjects in the training curriculum, except the international courses organized continuously by the Research Institute of Tuberculosis (RIT) Japan Anti-TB Association (JATA) since 1963. The RIT has incorporated social science subjects into the training curriculum for TB program managers from the start of training on the basis of the view that clinicians and TB program managers should apply a broader and more holistic perspective to TB services and TB programs. Currently, social science topics include concepts and practical examples about community beliefs and perceptions, social stigma, health systems and health-seeking behavior, gender, adherence to treatment, community participation and interpersonal communication skills. These topics are relevant to WHO's newly recommended Stop TB Strategy for achieving the MDGs [2].

CONCLUSION:

HIV/AIDS biologically and socially interacts with TB. Reducing TB associated HIV burden requires both biomedical and social interventions. The current involvement of social scientists in research and training for TB control in high HIV prevalence settings is limited. To facilitate the Millennium Development Goal for TB, social science research and training should be implemented in countries which are affected by these dual epidemics. Social science research can promote understanding regarding the complex psychosocial interplay of TB and HIV/AIDS. In addition to addressing these problems, social science research can help to identify the interventions which are effective in urging vulnerable patients, including women and the poor to take advantage of TB/HIV prevention and care services. Social science research should show how to implement these interventions on a large scale and how to influence national policy and care strategy [2,27,32]. The training courses designed for TB and HIV/AIDS program managers and service providers should include social science subjects to ensure that the program and services are responsive to the complicated biological and the psycho-social interactions of TB and HIV/AIDS.

ACKNOWLEDGEMENT:

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PROCEEDINGS OF THE 46TH ANNUAL MEETING OF JAPANESE SOCIETY OF TROPICAL MEDICINE

14-15 October 2005, Kyoto

President

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Special lecture

TREND OF JAPANESE FOREIGN AID IN EDUCATION —IMPLICATION FROM AFGHANISTAN ACTIVITIES—

SEIJI UTSUMI

Graduate School of Human Science, Osaka University

The turning point of educational foreign aid was World Conference of Education For All 1990 held in Thailand. EFA 2000 in Dakar and UN millennium Goals are refrain of EFA 1990. The EFA conference showed us the serious situation of education in developing countries.

The meaning of this conference is that the universal basic education becomes political goal from the ideology of education. After the EFA conference international aid went to the basic education field. The Japanese policy for educational aid mentioned in the JICA report of 'Development and Education' in 1994. There are 3 basic policies such as educational aid should be increased up to 15% of bilateral ODA, basic education should be main target, educational ODA should have well-balanced in all educational sectors.

1996 OECD-DAC announced the new policy paper of ODA, which were included educational goals. The DAC paper mentioned EFA goal should be cleared year 2015 and gender gap should be abolished up to year 2005. For clear these goals, MOF and JICA make the new educational policy paper which were included the making integrated developing plan with educational sector is needed.

Japanese government takes the initiative of Afghanistan reconstruction process includes education. Japanese educational support for Afghanistan had some different points comparer with before. Afghanistan aid had not only the development aid but also the emergency and the reconstruction activities. The Ministry of Education Japan took some initiative for implementing the activities with MOFA.

Now, Education Aid is 1 (one) billion US$ and 10% of total ODA (2002). This amount includes Yen loan and scholarship for foreign students. Technical cooperation of JICA educational budget is 30 billion yen and 20% of total JICA budget. JICA activities divide basic education vocational training and higher education one third each other.

After Afghanistan aid, Japanese foreign aid extends development aid to emergency and reconstruction. It means scheme, process and actor extend also. Ministry of Education, Universities and NGOs are new actor of this field. But they are not main actor yet. But now education is one of the main stream of ODA. Especially reconstruction stage of poet-conflict countries education is the most important field of support.

Therefore the following items are needed for the better educational aid.

Quality assurance of aid

Coordination and closer relation between various actors

Making comprehensive approach

Making system for emergency situation

Human development for educational aid

Prize Winner's lectures

The JSTM Award of Excellence

AN ENDEAVOR STUDY IN LABORATORY TO FIELD－A PERSONAL HISTORY, WHICH PASSES THROUGH A RESEARCH AND ERADICATION AGAINST ONCHOCERCIASIS AND LEISHMANIASIS－

SHIGEO NONAKA

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My concerned respected professor in dermatology, and parasitology was Dr. Michio Nogita, and Dr. Daisuke Katamine respectively. Their special interest in the field of study was the same origin, and actually they were the disciple followers of Dr. Seiichi Kitamura. Dr. Katamine was an alumni member of dermatology in Nagasaki university school of Medicine. My medical graduation was completed on 1965, and then served a rotating internship at Nagasaki university hospital for one year. After that, I got chance to get speciality training in the department of dermatology of Nagasaki University. During this period, Professor Nogita arranged all possible facilities for my training in dermatology, and Professor Katamine always encouraged me in all purposes to acquire knowledges. As a result, I entered into the postgraduate course, and carried out a biochemical study on acne vulgaris. After completion of my postgraduate course, the clinical training was carried out in dermatology clinics. My research exposure in the field of tropical medicine begun in a project for eradication of onchocerciasis in Guatemala, which was started by Dr. Isao Tada since 7^{th} decade of 20 century. I was engaged to acquire knowledge and experiences in a several subjects from this project not only dermatological, but also parasitological, epidemiological and entomological knowledges. Fortunately, at that time, I had opportunity to acquaint with the vast knowledges and experiences with my respected teachers of Dr. Yoshihisa Hashiguchi, Dr. Katsumi Aoki, and Dr. Takesumi Yoshimuri et al. However, I was engaged in this project for three years, and experienced clinically likely; onchocercoma, pretibial depigmentation, and onchocercal dermatitis etc. on this disease. After this project, I came back to join in my dermatology clinic. Eventually, my main interest of study is in the field of photobiology subject. From 1988, I joined again in a project of cutaneous leishmaniasis, which was started and still continuing by Dr. Yoshihisa Hashiguchi since 1986. For which, I already visited once or twice in a year to Ecuador for past 15 years with Dr. Y. Hashiguchi and other doctors. We had observed almost a thousand of patients with cutaneous and mucocutanenous leishmaniasis in Ecuador and Pakistan. Our research group carried out the extensive clinical, immunological, histopathological and molecular biological study of leishmaniasis. As a result, it could be possible for us to introduce a new diagnostic technique in the detection of parasites species specificity in leishmaniasis, clinical trials with new antileishmanial agents in the treatment of cutaneous leishmaniasis, and also invent a novel antileishmanial chemical agent for this disease. We already published our research activities in seven research series reports of studies on new and old world leishmaniasis, edited by Dr. Hashiguchi. I'm very proud of it that I had a good opportunity to participate on this report. Furthermore, I'm very pleased that my young colleagues are continuing on this subject of tropical medicine. I am optimist and confidant that Dr. Hashiguchi with his colleagues will have to continue their research works in future. Approximately 30 percents of my all published papers are concerned with the related tropical medicine and parasitological subjects. Finally, I am sincerely grateful to all members of Japanese Society of Tropical Medicine for their kind cooperation and heartiest support. Fortunately, I am going to retire on end of March, 2006, however I have great desire to continue my study, and also to educate our young dermatologists for necessity of investigations related in the field of tropical medicine subjects.

JSTM Young Investigator's Award

THE MECHANISMS OF THROMBOCYTOPENIA IN THE ACUTE PHASE OF SECONDARY DENGUE VIRUS INFECTIONS

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Severe thrombocytopenia and increased vascular permeability are two major characteristics of dengue haemorrhagic fever (DHF). To develop a better understanding of the roles of platelet-associated IgG (PAIgG) and IgM (PAIgM) in inducing thrombocytopenia and its severity of disease in patients with secondary dengue virus infection, the relationship between the PAIgG or PAIgM levels and disease severity as well as thrombocytopenia was examined in 78 patients with acute phase secondary infection in a prospective hospital-based study. The decrease in platelet count during the acute phase recovered significantly during the convalescent phase. In contrast, the increased levels of PAIgG or PAIgM that occurred during the acute phase of these patients decreased significantly during the convalescent phase. An inverse correlation between platelet count and PAIgG or PAIgM levels was found in these patients. Anti-dengue virus IgG and IgM activity was found in platelet elutes from 10 patients in an acute phase of secondary infection. Increased levels of PAIgG or PAIgM were significantly higher in DHF than those in dengue fever (DF). An increased level of PAIgM was associated independently with the development of DHF, representing a possible predictor of DHF with a high specificity. This data suggest that PAIgG, PAIgM involving anti-dengue virus activity play a pivotal role in the induction of thrombocytopenia and severity of the disease in secondary dengue virus infections. Of the 46 patients, the plasma thrombopoietin (TPO) levels in the acute phase were remarkably high, and it was decreased in the convalescent phase, although still significantly high level than those of healthy volunteers (HV). Since there are some reports that plasma TPO levels depend on the levels of the megakaryocyte in the bone marrow rather than the levels of peripheral blood platelets, we suggest that the thrombocytopenia in secondary dengue virus infections are also induced by bone marrow suppression. On the other hand, the levels of plasma vascular endothelial growth factor (VEGF) in the acute phase were significantly lower than those of HV, and they were recovered in the convalescent phase and they didn't show significant difference between DF and DHF. This data suggest that the plasma VEGF doesn't contribute to the increased capillary permeability. (Collaborator: Kazunori Oishi, Institute of Tropical Medicine, Nagasaki University)

Symposium 1

S1-1) THE DAWNING OF TRAVEL MEDICINE AND IMMIGRANT MEDICINE －INTRODUCTION－

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The travel medicine in Japan just started to established in academic field. And the area of these fields is not interest so much in Japanese.

Recently, Japanese overseas travelers are increasing over 1.700 million per year for the advancement of enterprise to the foreign countries and appreciation of Japanese yen. On the other hand, the foreign workers who work in Japan are increasing as a cheap manpower. These foreigners sometimes have diseases that are not only general diseases but also endemic diseases of the mother countries. However these foreigners sometimes cannot go in an enough medical treatment because of the difference of the language and culture. In Europe and America, the concept has already been established as an academic field named immigrant medicine in the travel medicine. First of all, we would like to discuss about “What is the location of immigrant medicine in the travel medicine? Furthermore, we will talk about the actual medical status for immigrant medicine in Japan, including in the deal with the foreign workers in the key hospital and clinical office in the region, and the current state of the medical interpreter who has established recently.

S1-2) MIGRANT MEDICINE IN TRAVEL MEDICINE

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Some people move from one place to another for pleasure, economic benefit, or academic interest, while others move out of necessity or because their old location is no longer safe. Such human movement is influenced by various factors, including environmental (climate changes, natural disasters), demographic (increase in the worldwide population), and socioeconomic ones (globalization of the economy, urbanization, easy access to information). These factors, intertwined in a complex form, have contributed to an increase in both migrants and travelers worldwide. Migrants often move from a poor country with a &quotone-way ticket&quot, and include immigrants, foreign workers, asylum seekers, refugees and undocumented immigrants, while travelers do so from a rich country with a &quottwo-way ticket&quot, and include tourists, business travelers, and expatriates. In 2003, the number of individuals living in foreign countries and the number of international arrivals worldwide are respectively 175 million and 700 million annually, which highlights the enormous volume of human movement currently occurring. Migrants face language/communication barriers, insufficient social acceptance, sequelae of tortures and violence experienced before arrival, and psychological isolation, and are thus prone to psychiatric disorders and drug/alcohol abuse in the receiving countries. Medical personnel seeing migrants need to possess numerous skills, including the ability to talk and communicate with migrants of different origin, to understand their personal history (including that of migration), to deal with different cultures, and to cooperate with other professionals (nurses, interpreters), not as one individual but as a member of a network. Medical issues that should be addressed include malnutrition (vitamin deficiencies), infectious diseases (TB, viral hepatitis, malaria), hereditary disorders (hemoglobinopathy), environmental disorders (lead poisoning) and post-traumatic stress disorders. For example, studies have reported that migrants arriving in Switzerland have a higher prevalence of TB, HBs-Ag and seropositivity for syphilis, and those who experience organic violence before arriving are more likely to have various somatic symptoms. In addition, countries receiving migrants may have to implement measures to prevent resurgence of some diseases. In Western countries, attention has been focused on health issues in VFRs (visiting friends and relatives). Because VFRs believe themselves to retain immunity to infectious

diseases that are prevalent in their home countries, they tend to neglect necessary precautions. The literature indicates that VFRs are more likely to contract malaria, typhoid and hepatitis A while traveling. Although this issue is not as serious in Japan as in Western countries, it appears to be steadily growing.

S1-3) RECENT TENDENCY OF IMMIGRANT MEDICINE AT HOSPITALS OF SHIGA PREFECTURE AND JAPAN

TAKESHI IDA

The meeting for International Medical Sevices, SHIGA (MIMSS)
Department of Surgery of Kohka Public Hospital

[INTRODUCTION and BACKGROUND] According to the statistics of Shiga prefecture (abbreviated as SP) of 2004, the registered foreigners in SP are 27,863 [Brazilians 12,856 (46.1%), Koreans (23.2%), Chinese (10.1%), Philippines (7.4%), Peruvians (6.7%) etc, which is about 2.0% of the whole population of SP]. But, the ratio of foreigners / Japanese in some cities is more than 5%. At the medical service zone of our hospital, 5361 foreigners are registered (3.8% of about 150,000 inhabitants).
[METHODS] The statistics documents of SP, local governments, Shiga International Association (SIAM) and our hospital, and reports at MIMSS.
[RESULT] Nine cities among local governments of SP, have consultation windows for foreigners-in Portuguses (9 cities), Spanish (1 city), English (4 cities) etc. They can give various advice, but cannot attend the medical scene. The rate of participation of national health insurance by foreigners is estimated to be about 40% in SP. The result of recent questionnaire about foreign language correspondence to doctors of main 5 departments of 63 hospitals at SP, there are extremely few doctors who can speak foreign languages except English. These languages are German (at 4 hospitals), French (1), Spanish (2), Portuguese (1), Chinese (2), Korean (5). We have an average of 1,000 outpatients / day in our hospital, and about 5-15 foreign outpatients / day. Operations of foreign patients during recent 8 years, were 207 cases, and the ratio of foreigners to the total cases in our hospital was about 1.2%. Of 207 cases, orthopedics was 31.2%, and surgery was 30.0%. In addition, there are also cases of HIV (AIDS), dengue fever,Chagas disease and the other uncommon diseases in SP. Therefore, it is necessary to take these diseases into consideration even at ordinary clinic and hospital.
[CONSIDERATION] Many foreigners living in Japan have difficulty in communication, cruel working conditions, health insurance non-participation etc. According to the study of S. Muraki. the number of foreign patients with difficult or impossible communication is estimated to be about 36,000 / day out of all foreigners living in Japan . In order to settle this a little, we developed a multilingual correspondence PC (joint development with Prof H. Matsuo of Kobe University , the affiliated hospitals and KDDI) , and got a good result .I also intend to introduce some recent trends such as medical interpreter authorization system, dispatch interpreter system and telephone interpreter system , which are studied by NPO or other groups.

S1-4) PROBLEMS ACCOPANIED WITH ACCEPTING FOREIGN PATIENTS IN SMALL MEDICAL FACILITIES IN JAPAN

YONEYUKI KOBAYASHI

Kobayashi International Clinic

From Jan.’90 to June ’05, 5982 foreign patients (totally 34902 patients),58nationals were checked at Kobayashi International clinic. Accepting foreigners in medical facilities, there are some problems. The first is language problem. English speakings are minority among foreigners in Japan. correspond to Spanish, Portuguese, Mandarin, Korean, Thai and so on is urgently. Understanding the culture and thinking way of them is the second problem. To make up confi-

dence through recognizing each other is only the way to perform adequate medical treatment. The third is financial problem. In general, foreigners are very easily suffering from financial problems comparing with Japanese. In addition, a part of the foreigners can't join or refuse to join Japanese official medical insrance system. Practicing Informed consent about the charge is important to avoid financial trouble. The fourth is difference of the diseases. For example, tropical diseases are very rare in Japan, so almost of the doctors in the small primary care facilities have seldom experiences not to misdiagnosis. Anyway, how to complete back up system for those 4 problems to help foreigners and doctors in small clinics is important.

S1-5) CURRENT PROBLEMS AND FUTURE SOLUTION IN MEDICAL INTERPRETATION/TRANSPLATION IN JAPAN

TOSHIHIRO MURAJI

AMDA-Hyogo, Hyogo, Japan

In multicultural society, as a product of the rapid globalization, public service interpretation/translation will be playing an important role for the foreigners with the divergent cultural backgrounds and language barrier to make a comfortable life in communities where they live. Convention interpretation/translation has been available in Japan, while the community interpretation recently became necessary in this era of globalization. Community interpretation/translation consists of judicial, medical, and administrative components. The characteristics of medical interpretation/translation are summarized in 5 folds; 1. advocacy associated, 2. Bidirectional interaction between the interpreter and client, 3. Information interpreted based on cultural background, 4. Volunteer based activities, 5. Ethical principles involved. Medical providers and on-going volunteer-based interpreters have been developing the training courses for medical interpreters /translators in the last several years. The curriculum of the course includes medical terminology, basic concept of each specialties, demonstration of hospital equipments and ethics to be considered as interpreters in health care. The medical interpreting/translation as one of the public service should be established for a proper training and licensing in an attempt to create our better society and to live hands in hands with foreign people.

S1-6) REPORT ON THE PRESENT STATUS OF THE MEDICAL INTERPRETER DISPATCH SYSTEM PILOT PROJECT IN KYOTO, JAPAN

AIRI TAKASHIMA

Kyoto Center for Multicultural Information and Assistance, Kyoto, Japan

Background: With the increasing number of foreign residents in Japan, concerns regarding health and medical care for those of limited Japanese language ability have been on the rise. This has led, in 2003, to the start of this medical interpreter dispatch system pilot project, with the cooperation of government administration, hospitals and a supporting nonprofit organization. The project dispatches interpreters of Chinese, English and other languages to hospitals which have agreed to the terms of the project. Each hospital selects a coordinator from among the hospital staff and provides medical liability insurance for the interpreters. Interpreting charges and transportation expenses are funded by government administration. The supporting group screens the applicants, and provides training and on-the-job supervision.
Purpose: Report on the present operational status of the Project.
Results: The system operated for 234 days in the year 2004, dealing with 1424 cases in which a total of 1102 people used the service. The departments where the service was most frequently used were neuro-internal medicine (12%), orthopedics (11%) and digestive tract internal medicine (9%). The interpreting services were used in a total of 1703 cases, for the explanation of symptoms and diseases in 1304 cases (76%), medical tests and/or examinations in 186 cases

(11%), and medication usage in 74 cases (4%). Before the start of the project, of the 38 nurses for outpatient surveyed 25 expressed concern about the accuracy of translation, 17 about the increasing number of foreign patients and 7 about possible problems arising from the interpreters lack of knowledge regarding patient medical history. At the end of the pilot project in 2004, of the 23 respondents, 11 expressed concern about the accuracy of translation, 10 about the interpreters' medical knowledge and 4 about patient confidentiality. While there have been requests for an increase of the number of days and hours, as well as interpreter availability for emergency cases, the problem of funding and financial assistance has yet to be solved.

Symposium 2

S2-1) MEDICAL COOPERATION FROM JAPAN TO AFRICA IN THE 21ST CENTURY; INTRODUCTION

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When we think about well-harmonized development of the world, it is a big concern to realize the situations in the sub-Saharan African countries. Problems in Africa are intricate in the origin, however, matters of health, especially infectious diseases, are one of the central issues. Through the recent political wind, Japan is requested to share responsibility to solve the problem in Africa. However, difficulties not only from geographical distance, but also in cultures, languages and other factors limited available human resources in Japan for cooperation with African countries. It is, therefore, obvious that we are facing an urgent necessity of development of human resources to be involved in activities in Africa. This symposium is conducted to discuss about the future strategy of the probable approach from Japan in the aspect of matters of Tropical Medicine. As the organizers of this symposium, we invited speakers from various areas; persons in political decision-making, in coordination of JICA projects, in NGO activities and in academia. Each speaker is requested to introduce the current situation and problems in respective project. It is important to have mutual understanding and cooperative scheme to promote effective international cooperation in Africa, because we realize that each component is not strong enough in Japan. Through the discussion, the organizers does not expect to have a tight conclusion about the role of the Japanese scientists in African issue, but we expect that each member of JSTM share the understanding the problem and start action needed for African issues.

S2-2) JAPAN'S CONTRIBUTION IN ACHIEVING THE HEALTH MDGS --- "HEALTH AND DEVELOPMENT INITIATIVE (HDI)"---

TARO YAMAMOTO

Deputy Director, Aid Planning Division, Economic Cooperation Bureau, Ministry of Foreign Affairs

The largest number of child preventable deaths is for malaria---- approximately one million deaths per year and the intervention with the largest single impact on reduction of childhood mortality is the distribution and use of insecticide treated bed nets. Their widespread use will result in: less burden on the health system; less out of pocket expenses; and improved work performance in adult.

The MDG 1 aims at eradication of extreme poverty: malaria is a disease of poverty, depriving Africa of up to $12 billion every year in lost GDP. Malaria is also clearly one of the major constraints for achieving the MDG 4 (Reduce Child Mortality) and 5 (Improve Maternal Health). Due to the high burden of malaria in Africa, where the disease causes about 25% of childhood deaths, malaria in Africa had to be addressed as an urgent priority in order to have any hope of achieving these goals. Thus, effective prevention of malaria with INTs impacts on almost all of the MDGs in one form or another. The same can be said for other infectious diseases including HIV/AIDS, tuberculosis and parasitic diseases. Health is thus the matter of threats to an individual as well as to societies. However, the progress toward achieving health MDGs (MDG4, 5 and 6: combat HIV/AIDS, malaria and other diseases) is lagging in many developing countries. For instance, regarding to MDG 4, we cannot presumably achieve more than a 42% reduction in the infant mortality rate (the target is two thirds=about 67% reduction) worldwide at the current pace. As for MDG 5, it is presumed that this goal will not be achieved except in Middle East and North Africa.

Based on above mentioned recognitions, the government of Japan announced early this year that Japan would provide 10 million ITNs by the year 2007, targeting children under 5 and pregnant women in Africa, with the expected outcome of 110,000 to 160,000 reduction in child death, and recently Japan announced new health initiative, called "Health and Development Initiative (HDI)," helping

achieve health MDGs with the financial contribution target of $5 billion over next five years (FY 2005-2009), in addition to $500 million pledge to Global Fund to fight AIDS, Tuberculosis and Malaria in the coming years, with the intention of doubling the Official Development Aid toward Africa in the next three years.

The full text of HDI is available on the web site as below: http://www.mofa.go.jp/policy/health_c/forum0506/hdi.pdf

S2-3) PRESENT SITUATION OF AIDS/HIV INFECTION AND ANTI-RETROVIRAL TREATMENT (ART) IN ZAMBIA: JICA HIV/AIDS AND TB PROJECT IN ZAMBIA

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First case of HIV infection was reported in Zambia in 1984. Thereafter, the government launched to fight AIDS through formulating National AIDS Prevention and Control Program followed by construction of The First Medium Term Plan (1988-1992), The Second Medium Term Plan (1994-1998) and National Strategic Framework (2001-2003). Despite these strategic efforts, situation of AIDS/HIV became worse with time in Zambia. The rate of the people living with HIV/AIDS in 2003 is estimated about 16.5% (UNAIDS, Epidemiological Fact Sheets, 2004) and nearly 2 million people are estimated to be infected with HIV among total population (11 million) in Zambia. Since the rate of dual infection of HIV and TB is very significant, the needs for HIV/AIDS and TB control are very high in this area. The Zambian government presents HIV/AIDS and TB control as public health priorities in the National Strategic Plan 2001-2005.

With this in mind, JICA launched the projects in Zambia from 1989. Present project was initiated from 2001 mainly in the University Teaching Hospital of University of Zambia as a major site to implement to improve status of HIV/AIDS and TB in Zambia. They include; 1) Transfer of laboratory techniques such as measurement of antibody and antigens, and CD4T cell counting, 2) Monitoring of ART drug resistance, and 3) Operational research against the patients with TB/HIV dual infection. The project purpose and overall goal are considered to be relevant and activities are sufficiently achieved in terms of the needs of Zambian health sector, Zambian government policy and Japanese ODA policy.

Status of AIDS/HIV and ART carried out in Zambia based on 3 by 5 program and our strategies through JICA project will be presented.

S2-4) THE PROSPECTS FOR THE MALARIA CONTROL, USING BY HOME BASED AND SCHOOL BASED APPROACH, IN AFRICA

JUN KOBAYASHI

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I would like to recommend that the home based management of malaria treatment and school-based malaria education are a useful additional strategy to strengthen the malaria control program in Africa. The global strategy of malaria control in recent years was made on the basis of the PHC; primary health care management. In the strategy, the strengthening for public health facilities and village volunteer in the community are main tools to improve the treatment and the prevention of malaria. However, malaria in African countries have still been a serious public health problem in spite of the efforts to carry out the control programs, which was modified from the global strategy, because of the following factors; hard accessibility to health facilities, poverty, lack of confidence in health facilities be-

cause of the problem for the quality of health services and lack of uniformity of the service by the community health volunteer. In this situation, the home based management for malaria treatment is attracting attention because the strengthening the treatment to the children by their mother is effective as an early treatment despite uncertainty of diagnosis and treatment. Thus, the private sector such as a pharmacy and a local shop has a share to scale up this strategy. Malaria control using by the insecticide treated bed net has remained as a tool of the poverty reduction in Africa, thus, the behavior change communication to use bed net should be strengthened. The school based malaria control was evaluated as a new tool of behavior change communication to the communities in Southeast Asian countries. This new strategy promotes the schoolchildren as a health messenger to the community using by Participatory Learning Action in the education. Regardless of the low rate of the pupils in the community in the Africa, the school-based approach might be effective as a behavior change communication.

S2-5) THE ROLE OF COMMUNITY HEALTH WORKER IN INFECTIOUS DISEASE PREVENTION IN SENEGAL

CHIKAKO SHIINA[1], NDEYE AMY BATHILY[2], ABOUBACRY FALL[2], MAYUMI SHIMIZU[1], REIKO HAYASHI[3]

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[2]Ministry of Health and Medical Prevention, Dakar, Senegal
[3]Linz Co.Ltd, Tokyo, Japan

[Introduction] The purpose of the JICA Project for the Development of Human Resources in Health, Republic of Senegal, is to strengthen the system for educating health personnel working in primary health care facilities. The project is being implemented in three sectors from November 2001 to October 2006. Activities in the sector concerning training of community sanitary agents (ASC: Agents Sanitaire Communitaires) are aimed at establishing an appropriate training system in the test area (Fatick Region, Sanitary District of Gossas). [Outline] In Senegal, the end institutions of primary health care are the health huts where the ASC educate residents, treat wounds and handle basic drugs. The present situation is such that the ASC working in the health huts focus mainly on treating wounds and administering basic drugs and little emphasis is given to educating residents. [Method]ASC training for 32 trainees from 32 villages in Gossas district was held at 9 health posts for 3 months. The trainees were instructed in the necessity and methods of educating residents by the health post chiefs (state nurses), using the ASC training manual. After the training, the health post chiefs regularly visited the ASC and health huts to provide guidance. To promote control of infectious diseases, ASC education activities included teaching residents about insecticide-treated mosquito nets to prevent malaria, educating them about HIV/AIDS, promoting vaccinations and administering medicines against worms. [Results] As of July 2005, all 32 ASC were engaged in health work one year after the training. Of the 32, 17 regularly undertake education of residents. By the end of May 2005, all 640 insecticide-treated mosquito nets distributed to the health huts in the 32 villages had been sold to residents. [Consideration]Together with the commitment of the health administration, ASC are essential to infectious disease prevention among residents.

S2-6) PREVAILING ESSENTIAL MEDICINES IN AFRICA

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Access to essential medicines has improved considerably during the past quarter century, but is still inadequate for one-third of the world's population. Not only antiretroviral drugs, but even ordinary medicines, such as

remedies against respiratory infections and diarrhea, are unavailable to many of these people. According to the WHO, only 50-80% (’99) of people in Cote d’Ivoire, one of the most prosperous countries in Africa, have regular access to essential medicines and the situation is much worse in many south Saharan countries. The reasons include immature infrastructure and weak regulatory control. Every stage from development to manufacture, distribution and use of medicines is well controlled in developed countries, as it has been learned that low-quality medicines directly threaten human life. However, only a third of Medicine Regulatory Authorities (MRAs) in the world are functioning properly, while another one third are not fully adequate, and the rest are ineffective or absent. We show here that inadequate control leads to loss of public confidence in pharmaceuticals. By means of authenticity investigation in collaboration with MRAs and manufacturers, we investigated the authenticity of 353 pharmaceutical samples, consisting of anthelmintics, antibiotics and antipyretics, collected in July 2004 in Cote d’Ivoire. Medicines were sold not only by licensed pharmacies, but also by unlicensed street shops and street vendors. The latter sold medicines at one-fifth lower prices than the pharmacies. Out of 353 samples, only 75 (21%) had authorization from the DMP (MRA of the Cote d’Ivoire) and 278 (79%) did not. All medicines sold at pharmacies had authorization, while 95% of medicines from street sources did not. Two authorized medicines (3% of 75) were identified as counterfeit, while 49 unauthorized medicines (18% of 279) were counterfeit. Without in-depth investigation, it is impossible in most cases to distinguish counterfeit medicines from authentic ones. Robust regulatory control of medicines, such as licensing of pharmaceutical selling and authorization of medicines, is indispensable to ensure trustworthy medicines for medical professionals and patients. Furthermore, dispensing of prescription medicines, such as antibiotics, without prescription may well lead to the development of resistance. It is important to promote rational use of medicines. Considering the scale of the problem, it is necessary for countries to develop a comprehensive master plan covering access, quality and rational use of medicines for the pharmaceutical sector and for pharmaceutical management, and to implement it vigorously. We appreciate cooperation of concerned MRAs, manufacturers, PSI and WHO.

Symposium 3

S3-1) THE ROLE OF LABORATORY IN INTERNATIONAL COOPERATION IN THE FIELD OF TUBERCULOSIS AND HIV CONTROL

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A third of the 40 million people currently living with HIV in the world are also infected with TB bacilli. The co-infection rate is much higher in the sub-Saharan Africa. Once those already infected with TB bacilli also become infected with HIV, they are approximately 10 times more likely to develop TB disease than those without HIV infection. Since 60% of the people infected with HIV globally live in the sub-Saharan African countries, the TB cases in this region are on the increase. Many of them die of TB. In 2003, the incidence rate of TB in the world decreased except in the WHO African Region. On the other hand, while a third of the world population is estimated infected with TB bacilli, most of them are living in populated Asian countries. HIV infection is rapidly spreading in Asia in recent years. Not only limited in sub-Saharan Africa, TB/HIV co-infection is becoming a major concern in Asia as well. To control TB, the WHO introduced a new strategy called DOTS in early 1990s. As of 2003, DOTS reached 77% of the entire population in the world. More than 80% of those diagnosed with TB have been successfully treated. For HIV/AIDS control, the introduction of the ARV in developing countries has revolutionized the HIV strategy. With the 3 by 5 initiative of the UNAIDS/WHO, the ART (treatment with ARV) has become possible. Financial support to carry out effective TB and HIV control in the developing world has also been made available. Following the Infectious Disease Initiative declared during the Okinawa summit in 2000, the Global Fund to Fight AIDS, malaria, and TB was established in 2002. Once the infectious disease control with the adequate treatment and the financial support is made possible, the capability of a laboratory becomes crucial. For instance, the CD4 count is necessary to determine when to start ART. Monitoring of the drug sensitivity also becomes important. The well functional laboratory is needed to properly diagnose various opportunistic diseases. For the TB control, in addition to the sputum smear examination and its quality control, the drug sensitivity test and other advanced technological development is also needed. How to integrate the public health strategy for infectious disease control with the adequate laboratory technology has become crucial in international cooperation for TB and HIV control.

S3-2) TB/HIV FIELD RESEARCH ACTIVITIES IN CHIANG RAI, THAILAND

NORIO YAMADA, HIDEKI YANAI

The Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, Tokyo, Japan

Chiang Rai Province, Thailand, is the area which had seen a HIV epidemic in the 1990s. Due to the HIV epidemic, tuberculosis incidence had increase since early 1990s. To deal with tuberculosis, Research Institute of Tuberculosis (RIT), Japan Anti-tuberculosis Association, started TB/HIV Research Project in collaboration with Thai Ministry of Public Heath and other organizations. In this presentation, we report the project activities focusing on the role of laboratory. One of main objectives of the Project is epidemiologic researches of TB in HIV prevalence areas. As a core project activity, a population-based surveillance of tuberculosis was set up and provincial TB registry data since 1987 including treatment outcome was computerized. HIV voluntary counseling/testing and drug sensitivity testing were instituted and have been an integral part of the surveillance system since 1996. Because proportion of smear negative tuberculosis and proportion of MOTT in HIV infected population is higher than in HIV uninfected population, culture examination is important in HIV high prevalence areas. To monitor the trend of drug resistance TB, the project has established TB laboratory system through collaboration with the national tuberculosis reference laboratory of Thailand. Solid media based culture laboratory for primary culture is carried out at the provincial hospital and

isolates are transferred to the national reference laboratory for identification and drug susceptibility examinations. Recently liquid media culture system has been introduced for further improvement of TB laboratory through collaboration among US-CDC, Thai MOPH and the project. Using the isolates, to assess the transmission dynamics of TB in the HIV high prevalence area, RFLP examination has been carried out in collaboration with Mahidol University. Other objectives of the project include researches related to health service of reducing TB incidence and mortality of HIV co-infected TB. CD4 measurement is carried out with a flow-cytometer donated to a community hospital by Japanese Government. Examination of blood concentration level of anti-retroviral medicines and viral load, which is required for studies of anti-retroviral medicines for HIV co-infected TB patients, is carried out in the facility of Thai Red Cross HIV research. For virologic studies of HIV, collaboration with Thai NIH, Bangkok and Medical Science Centre in the province has been established. The laboratory system is required for not only biomedical but also epidemiologic studies of TB/HIV as mentioned above. It is though important to establish collaboration with local organizations having laboratory in middle-income countries like Thailand.

S3-3) A MOLECULAR ANALYSIS OF TUBERCULOSIS INFECTION IN ZAMBIAN PRISONS

SATOSHI MITARAI

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Japan Anti-Tuberculosis Association

A molecular analysis of tuberculosis infections has been conducted in Zambian prisons. The consecutive 3 sputum samples were collected from the inmates of 14 prisons with respiratory symptoms through June 2000 to January 2001. A total of 1,050 inmates were enrolled into the study and 3,130 specimens were collected. The male proportion was 98% and mean age was 30.2±8.1. A total of 259 *M. tuberculosis* strains were isolated and 101 strains were analysed using standard restriction fragment length polymorphisms (RFLP) and resistance ratio drug susceptibility testing method, subsequently. The strains conformed 18 clusters and the size varied from 2 to 22. The major 2 clusters were considered as most prevalent *M. tuberculosis* strains in Zambia. In each prison, several inmates in a same cell had pulmonary tuberculosis and the *M. tuberculosis* isolates showed same RFLP pattern. Majority of the clusters to which the inmates belonged were cluster 1 or 2. They might be a reflection of general prevalence of tuberculosis in the community and the patients seemed to be infected outside the prison. However, two inmates in Maximum Kabwe prison had tuberculosis that pathogens classified into rare cluster, and it seemed to be an intra-cell infection during the custody. In general, the conditions in prisons in developing countries are terrible and a few countermeasures are taken to prevent the dissemination of any infectious diseases. The high prevalence of tuberculosis in prisons is mainly due to outside infection, but a part of them could be infected and developed in the prison. Any countermeasure must be taken to prevent an outbreak of tuberculosis in prison and to diagnose the patient in an immediate manner.

S3-4) HIV SEROPREVALENCE SURVEY AMONG TB PATIENTS IN CAMBODIA (2003 AND 2005)

NAMIKO YOSHIHARA

The Research Institute of Tuberclosis Japan

Not received

S3-5) WHERE ARE GOING LABORATORY PROJECTS IN DEVELOPING COUNTRIES? —THE CASE OF HIV/AIDS & TB CONTROL PROJECT IN ZAMBIA—

NAOMI WAKASUGI

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In Europe “Hospital” came into existence in 17th century, and in 19th century the pathogens of infectious diseases have been discovered by Pasteur, Koch and other scientists in succession.

At the same time Tropical Medicine has been developed, which was the root of international cooperation with laboratories in developing countries nowadays. Calmette produced a laboratory in Saigon in Vietnam in 1891 as the first Pasteur institute overseas, and then Yersin went to Hong-Kong and worked for Pest research in a laboratory like a shanty in 1894. Since then Pasteur institute has continued the existence of about 30 laboratories in developing countries for more than 100 years.

Looking at international medical cooperation from Japan, we have a certain history of laboratory project in developing countries. Particularly it should be noted that the main technical assistance to African countries has been implemented into laboratories such as Noguchi institute in Ghana, KEMRI institute in Kenya and UTH laboratory in Zambia by producing new laboratory or strengthening existing laboratory, developing research and building human capacity. These laboratories lasted for more than 10 years, and whether and how these should be continued is being discussed now. The decision should be done very carefully when the role of laboratories has become important more and more in Africa facing a serious threat of AIDS and TB and the start of global initiative for care and treatment.

In Zambia JICA started a technical cooperation with University Teaching Hospital (UTH) by establishing viral laboratory in 1989 and served as a base for the surveillance of and research for infectious diseases. On the other hand its research-oriented way of cooperation has been criticized. However the third-phase project since 2001 named HIV & TB control project in Zambia has focused on two main objectives: 1. To strengthen and sustain UTH laboratory and countrywide laboratory system. 2. To utilize effectively the capacity of the laboratory to national HIV & TB control. The activities with particular mention are: 1. Countrywide expansion of less expensive CD4 count method. 2. External quality assurance of sputum smear testing for TB. 3. Operational research for community-based ARV therapy to HIV/TB coinfected people using DOTS.

The comments will be presented on how should be the future of laboratory project in Africa, what is the barrier to the continuity, how should we address laboratory project with what understanding of its role and importance.

Symposium 4

S4-1) WHAT ARE VECTORS? HOW SHOULD WE CONTROL THEM?

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Vector-borne diseases are still one of major issues in tropical medicine. Their transmission dynamics looks only slightly different from other common infectious diseases, of which transmission cycles consist of two organisms, host and agent (pathogen). However an additional third organism, such as mosquito, tick, snail, and so on as vectors makes more complicate the transmission dynamics of the vector-borne diseases. Analysis in mutual interaction among these organisms and the functional response of each organism against environment need a flexible approach beyond the host-parasite relationship. Therefore scope to vector-borne diseases should be deepened only when we spire our interest to not only medical science but also to biology, especially to ecological achievements based on interdisciplinary approach. This symposium hopefully provides recent scientific information on the mode of change in epidemics of malaria, dengue fever, schistosomiasis, and tick-borne diseases, all of which might be caused by the adaptive changes in local vector or intermediate host populations reacting to natural and socio-economic environmental changes. Yielding environmental friendly vector/intermediate host control strategy is the key concerns toward the control of vector-borne infectious diseases.

S4-2) LIFE HISTORY ADAPTATION AND TRANSMISSION OF HUMAN DISEASES IN MOSQUITOES

YOSHIO TSUDA

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Aedes aegypti is the most important vector of dengue fever in Southeast Asian countries. This species has originated in central Africa and two subspecies are distinguished. One is a sylvan form, Ae. aegypti formosus, found in forest and the other one is a domestic form, Ae. aegypti aegypti, found in domestic habitat. It is proposed that dengue virus may have originated in a forest cycle in Southeast Asia. The domestic form Ae. aegypti aegypti has a good ability to adapt to domestic environments and established a close relationship with human throughout tropics. Therefore, this species becomes an efficient vector of human diseases, such as dengue fever, yellow fever, filariasis etc, in tropical countries. Since no vaccine is available now for dengue fever, the basic strategy of dengue control based on the vector control, especially the source reduction. To effectively reduce larval population it is necessary to know key containers of the target area through a house survey. From January to February 2005 a big outbreak of dengue hemorrhagic fever occurred in Dili, East Timor. Results of vector situation survey showed that plastic bottles of 5-liter volume, drums and used tires were the main breeding sites of Ae. aegypti in Dili, and control measures focused on these breeding sites were recommended as the first stage of the vector control. The vector situation surveys conducted in Southeast Asian countries showed that kind and the composition of containers used for larval breeding of Ae. aegypti differ greatly among localities because of the difference in climate, economic conditions, and life style. There is a significant change in the composition and relative importance of containers after an effective control of breeding sites. Some containers less important for larval breeding before are preferred for oviposition and the relative importance of these containers for larval breeding becomes higher. This breeding site shift might be the result of adaptive changes in life history of Ae. aegypti.

S4-3) AFRICAN MALARIA VECTORS AND THEIR RECENT STUDIES

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The major malaria vectors in Africa are *Anopheles gambiae, A. arabiensis* and *A. funestus. Anopheles gambiae* and *A. funestus* are relatively more anthropophagic and endophilic than *A. arabiensis.* Larvae of *A. gambiae* and *A. arabiensis* frequently occur in small, temporary and open habitats. The egg to adult duration of *A. gambiae* and *A. arabiensis* is usually 7-10 days under the optimal condition. Breeding sites of *A. funestus* are limited to large water bodies with aquatic vegetation, and they require a few weeks to mature. *Anopheles gambiae* and *A. arabiensis* are difficult to separate morphologically for both adults and larvae, therefore, they were treated as *A. gambiae* s.l. in past studies. Since the mid 90's, these two species have been identified using the rDNA-polymerase chain reaction (PCR) method. A recent biogeographical study using the PCR method reported that *A. arabiensis* was not found in the highland area above 1400 m elevation in western Kenya, and *A. gambiae* was not recorded in the Great Rift Valley. The result suggests that *A. arabiensis* is more adapted to dry climate than *A. gambiae*. Studies in population genetics also found that populations of these three species are genetically separated by the Grate Rift Valley. Since the late 80's, malaria epidemics have occurred in multiple sites in East African highlands (above 1500 m). Several hypotheses have been proposed to explain the increased malaria transmission in the highlands, including land-use changes and global climate changes. Recent studies suggest that global warming is not directly related to highland malaria. Although malaria parasites influence lifespan and fecundity of mosquitoes, the studies have conflicting results, and more research is needed in the interactions between mosquitoes and parasites. To reduce malaria incidence, insecticide-treated bed nets are effective. However, the nets have to be used continuously in a large area. For larvicides, the environmental safe toxin from *Bacillus thuringiensis var. israelensis* and *B. sphaericus* has been considered. Studies in genetically modified mosquitoes (GMM) have been also active, but application of GMM is still far from reality.

S4-4) INTERMEDIATE HOST SNAIL OF SCHISTOSOMIASIS

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The application of chemical compounds, toxic to the intermediate host snail, was the main measure of control for schistosomiasis before using prazuquantel. When praziquantel was introduced, it became the drug of choice in the great majority of endemic countries. However, the information for the intermediate host snail is still essential for the control of schistosomiasis. I show some facts for intermediate host snail with an expectation in the increase of interest in snails. Snail population number and transmission cycle: Fluctuations in snail populations, the rate of infection and the production of cercariae are generally strongly influenced by the climate. The information on snail populations and transmission cycles is indispensable for the selection of treatment times. Competition between snail species: Members of Ampullariidae and Thiaridae have been successfully tried as competitors of Biomphalaria spp. in many of the West Indian islands. Various species of aquatic snails are effective as decoys or sponges to intercept schistosoma miracidia. Environmental management: We attempted to control snail population in Mwachinga and Mtsangatamu villages in Kenya. In Mwachinga village, the river dries up in the dry season, with the subsequent formation of small pools. Towards the end of the dry season, these pools dry up completely. However, snails can survive under the vegetation which maintains an appropriate humidity. Snails in the pools were eliminated by scooping, and the river bed was dried by clearing the vegetation. In Mtsangatamu village, the modification of river streams was carried out in the part of river of which the flow is perennial. The snail habitats were reduced by the clearing of water plants and concentrating the stream water into a narrow channel.

S4-5) VECTOR ECOLOGY AND PREVENTIVE STRATEGY FOR TICK-BORNE EMERGING/REEMERGING DISEASES IN ASIA

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Outbreaks of tick-borne emerging/reemerging infectious diseases are depend on vector competence of tick fauna in each one of endemic areas. But vector survey and preventive strategy are not easy to complete in each area, because of complicated factors; double vector species, genetic polymorphology of pathogens, tick habitats associated with geology and climate, irregular prevalences of pathogens among reserviors and latent infection among local inhabitants. Herein, vector competences of spotted fever, Lyme disease and babesiosis are presented from geopathological and genetic epidemiological viewpoints on a relationship between the Japan Islands and Asiatic Continent. Based on our surveys, new information as follows; southern limit of northern species Ixodes persulcatus, wide distribution of Asian species Ixodes ovatus and southern species Ixodes granulatus, unexpected diversity of spotted fever group common to Japan and Asiatic Continent, migratory birds-borne Lyme borreliae in Far East, diversity of rodent-borne babesiae in Japan and southern China. Thus, tick vector ecology is comfused arround Asia including Japan. To make a plan for preventive strategy to tick-borne infectious diseases, I propose to integrate various information on tick vectors in Asia, such as a map of ticks and diseases with reference to geological information system (GIS) with computerizing, and colaboration with any medical support projects to Asian countries.

Workshop C-1

14C-01) THE SPLENOMEGALY OF NC/NGA MICE INFECTED WITH *PLASMODIUM BERGHEI*

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About for the splenomegaly which happens in case of malaria infection, it compared and examined ddy mice and NC/Nga mice. *Plasmodium berghei* which were imparted from Teikyo University and it is subcultured in our laboratory for more than 20 years were used in all experiment. When inoculating the blood of the infected mice intraperitoneally to ddy mice, the splenomegaly becomes remarkable at the 4th day of infection and reaches in the maximum at the first week of infection but the majority of mice died at this point. When administering Fansidar to the mice at the 4th day of infection, the malaria parasite in the blood disappeared but the splenomegaly of the treatment mice at the first week of infection were approximately as equal to those of the untreated mice at the first week of infection (It compares at the spleen/body weight ratio). In the meantime, when the similar examination was done using the NC mice, the spleen/body weight ratios of normal NC mice were significantly smaller than those of normal ddy mice, and those were increased at the first week of malaria infection even to almost equivalent with the spleens of normal ddy mice. The majority of malaria infected NC mice also died in the first week of infection. When the mice were treated by Fansidar at the fourth day of infection, the malaria parasite in the blood disappeared and the spleen/body weight ratio almost equivalently increased with the enlarged spleens of ddy mice of the first week of infection.

It is known generally that the degree of the splenomegaly in malaria infection differs by the strain of mice, and the relationships between the defence mechanisms were reported. In present experiment, because the splenomegalies in the infected mice were slighter even in NC mice than ddy mice, the possibility in which some disadvantages occurred to the organism was considered. However the clear difference could not be found in the change of the parasitism in malaria infection and the death time in both mice. In future we want to examine the reason why the splenomegaly of NC mice almost equivalently increases with the ddy mice after the malaria treatment.

These results were recognized in fortuity in the experiments of malaria infection which were given as the problems to the students of the selection class throughout several years, and we want to thank them.

14C-02) GENE CONVERSION AND EXTENSIVE POLYMORPHISM OF THE RHOPH1/CLAG FAMILY MEMBERS IN *PLASMODIUM FALCIPARUM*

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The *Plasmodium falciparum* high molecular mass rhoptry protein (*Pf*RhopH) complex is important for parasite growth and comprises three distinct gene products: RhopH1, RhopH2 and RhopH3. *P. falciparum* RhopH1 is encoded by members of the previously- termed *clag* (cytoadherence-linked asexual gene) multigene family that we have now renamed as *rhoph1/clag*. Because the polymorphism of the pathogen protein contributes an evasion from host immunity, we determined the nucleotide sequences corresponding to the open reading frame for five *rhoph1/clag* members, *rhoph2*, and *rhoph3* in 4 culture-adapted lines (approximately 113 kb total). Sequences were compared with those from the 3D7 parasite line in the genomic database. We found that among seven genes, *clag9*, *rhoph2* and *rhoph3* were relatively less diverse, similar to the other known rhoptry proteins, such as *rap-1*. However four *rhoph1/clag* members were highly polymorphic comparable to the micronemal proteins when full length sequences were compared. Interestingly, all of four *clags* show the highest diversity at amino acid 1000-1200 and the degree is comparable to the diversity observed in the molecules exposed on the merozoite surface, such as *merozoite*

surface proteins-1 and *-2*. Additional sequences of the polymorphic region in four clags in more than 20 parasite lines illustrates the extensive diversity of this region, which were never observed in the molecules located in the apical organelle of merozoites. The gene conversion event was detected between the most diversified *clag3.1* and *clag3.2*, which might serve as a driving force to accumulate polymorphism. Furthermore in several culture-adapted parasite lines, regions between *clag3.1* and *clag3.2* were not detected from gDNA probably due to a recombination event between the two closely related *clag3* genes. The highly polymorphic nature of the RhopH1 suggests that the RhopH complex is under selective pressure and RhopH1 is the target domain.

14C-03) STRUCTURE AND EXPRESSION ANALYSIS OF A MULTIGENE FAMILY OF GP82 OF *TRYPANOSOMA CRUZI*

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The infective forms of *Trypanosoma cruzi*, the causative agent of Chagas disease, are metacyclic trypomastigote form in excreta of triatomine vectors and trypomastigote in the blood stream of mammalian host. Metacyclic trypomastigotes express stage specific glycoprotein 82kDa (gp 82). The gp 82 is involved in the invasion of parasites into the host cells by inducing Ca^{2+} signal in target cells by the attachment with cadherine. The functional gp 82 is suggested to be member of a multigene family related to the trans-sialidase family. To investigate the role of gp82 in pathogenesis, we studied gene structure and expression of gp82 in the human isolates, Peru 1 and Peru 2 strain derived from Peru, We amplified the gp82 gene using specific primers, cloned into E. coli. Then restriction fragment length polymorphism (RFLP) of 25 clones of the gp82 full length of PCR fragments from genomic DNA of each strains was analyzed after EcoR I and Hind III digestion. The result showed that A, B, C, and E different restriction fragments patterns were found in Peru 1 and Peru 2 strains. We further estimated the copy number of the A, B, C and E types genes in the PCR products by using cloning and PCR specific primer for each type. A, B, C and E types were found 4%, 13%, 8% and 61% clones in Peru1and 1%, 12%, 15% and 43% clones in Peru 2 respectively. Another type (similar E) of gp82 (13 from Peru 1, 24 from Peru 2) was also detected by this analysis. The full length DNA sequencing analysis revealed that inter-types homology was 95～98%. and the intra-types homology was 85%. We studied expression level of detection types of the gp82 gene in epimastigote and metacyclic trypomastigote stages by using real time PCR. We compared the expression levels of the different stages of *T. cruzi*, normally epimastigote and metacyclic each types of gp82 gene by using actin gene expression as control Within the multiple genes belonging to the same gp82 family, type C gene was some how specifically activated at the metacyclic stage and the expression levels of the gp82 genes were suggested to be independent from the copy number in the genome.

14C-04) CRYSTAL STRUCTURE AND CATALYTIC MECHANISM OF *TRYPANOSOMA CRUZI* DIHYDROOROTATE DEHYDROGENASE

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Chagas disease (American trypanosomiasis) is caused by the flagellate protozoan parasite *Trypanosoma cruzi* (*T. cruzi*) and affects approximately16to18million people in Central and South America. A large percentage of Chagas patients receive no specific anti-parasitic therapy because of the ineffectiveness and toxicity of existing pharmacologic agents. Hence better therapeutic agents are urgently needed. Dihydroorotate dehydrogenases (DHODs) are flavoenzymes catalyzing the oxidation of L-dihydroorotate (DHO) to orotate, the fourth step and the only redox reaction in the de novo pyrimidine biosynthesis pathway. *T. cruzi* DHOD (TcDHOD) is a cytoplasmic enzyme and utilize fumarate as physiological oxidant suggesting that it is involved not only in the de novo biosynthesis of pyrimidine but also in redox homeostasis of the parasite. In contrast, human DHOD is attached to inner mitochondrial membrane and utilize respiratory quinones as physiological oxidant. This great diversity between parasite and host DHODs makes this enzyme a potential target for new chemotherapeutic drugs. Determination of the structure of TcDHOD should help in the development of new TcDHOD-specific drugs. This should also help to clarify the catalytic mechanism of dihydroorotate oxidation by family 1A DHODs. Here I report the X-ray structure analyses of native TcDHOD and the enzyme complexed with substrate and products such as DHO, orotate, fumarate, succinate and an inhibitor oxonate. These structural data confirmed at atomic level the ping-pong Bi Bi mechanism proposed for TcDHOD and it will definitively help to understand the proton and electron transfer steps of the DHODs in much greater detail.

14C-05) MUTATIONAL ANALYSIS OF TRYPANOSOME ALTERNATIVE OXIDASE (TAO) AS A POTENTIAL TARGET FOR TRYPANOSOMIASIS CHEMOTHERAPY

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African trypanosomiasis, or more commonly known as sleeping sickness in humans and nagana in cattle, is caused by a trypanosome parasite infection, and is transmitted by tsetse fly. Trypanosome alternative oxidase (TAO) of African trypanosomes is an ideal target for medicinal chemotherapy, since it dose not exist in host mammals. We have previously shown that antibiotic ascofuranone, which is isolated from phytopathogenic fungus, *Ascochyta visiae*, was found to specifically target this enzyme, indicating that the site of inhibition is the same or close to its quinol substrate binding pocket. In this study, we have identified residues that are involved in the active site of the recombinant *Trypanosoma vivax* alternative oxidase by alanine-scanning mutagenesis. Using multiple sequence alignment of mitochondrial alternative oxidase (AOX) including TAO and plastid alternative oxidase (PTOX), we have identified a strong conservation of a glutamate and a tyrosine residue with 6 amino acids apart and an existence of the important motif of -E(X)$_6$Y- . The alanine scanning mutagenesis of glutamates and tyrosines has revealed that the essentiality of those residues is highly specific. We have concluded that the -E(X)$_6$Y- motif consititutes in the active site of the enzyme, as similarly in the group of other membrane-bound diiron carboxylate proteins, which are previously reported.

Our results have indicated a more detailed picture of the active site of TAO. More detailed analyses are underway to identify the enzyme's active site, which can potentially become the site to be inhibited by a drug.

14C-06) ROLES OF CD8$^+$ T CELLS FOR ACHIEVING THE CONTROL OF *TRYPANOSOMA CRUZI* INFECTION

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Trypanosoma cruzi (*T. cruzi*) is the etiological agent of Chagas' disease in Central and South America. We previously identified a major epitope of trans-sialidase surface antigen (TSSA) recognized by CD8$^+$ T cells in *T. cruzi*-infected C57BL/6 mice and have demonstrated that vaccination with plasmid DNA encoding TSSA can induce CD8$^+$ T cell-mediated protective immunity against lethal *T. cruzi* infection. Vaccination using recombinant viral vectors has become a promising strategy to induce T cell immunity against intracellular infectious agents. Adenovirus and vaccinia virus have been shown to be the most efficient vectors for inducing protective immune responses against several infectious diseases. In the present study, we demonstrated that vaccination with recombinant adenoviral and vaccinia viral vectors expressing a single CD8$^+$ T cell epitope, ANYNFTLV, which is derived from a *T. cruzi* TSSA antigen, was effective for protecting mice from lethal *T. cruzi* infection. We also found that recombinant vaccinia virus expressing receptor activator of NFκB (RANK) ligand exhibited an adjuvant effect for enhancing the induction of ANYNFTLV-specific CD8$^+$ T cells. These findings demonstrate that the immune response directed against a single CD8$^+$ T cell epitope is sufficient for controlling the lethal *T. cruzi* infection, providing a new basis for improving vaccine strategies against Chagas' disease.

14C-07) DEVELOPMENT OF TWO-STEP DNA VACCINES TARGETING THE LIVER-STAGE MALARIA PARASITES BASED ON THE UBIQUITIN-PROTEASOME SYSTEM

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CD8$^+$ T cells have been implicated as critical effector cells in protection against preerythrocytic stage malaria. We have reported that DNA vaccines encoding an ubiquitin-fused antigen preferentially induce the main effector CD8$^+$ T cells through efficient protealysis mediated by the ubiquitin-proteasome pathway. In this study we constructed plasmids encoding ubiquitin-fused circumsporozoite surface protein (CSP) and ubiquitin-fused merozoite surface protein 1 (MSP1), respectively, and co-immunized the mice with these two plasmids , then challenged with sporozoites of lethal plasmodium yoelii strain. These two-step DNA vaccines are expected to induce protective immune responses mediated by CD8$^+$ T cells, targeting the hepatocytes infected with early sporozites or merozoited just before release. The roles of antigen-specific antibodies , INF-gamma, CD4$^+$ T cells and CD8$^+$ T cells will be investigated, and the immune responses after challenge the immunized mice with sporozites and merozites will be compared.

14C-08) SIGNALING MOLECULES RESPONSIBLE FOR THE EXCYSTATION AND METACYSTIC DEVELOPMENT OF *ENTAMOEBA INVADENS*

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Using an axenic excystation system in vitro, we examined the effect of protein kinase C (PKC) and phosphatidylinositol 3-kinase (PI3K), which are signaling molecules responsible for numerous cellular responses, on the excystation and metacystic development of *Entamoeba invadens*. Excystation, which was assessed by counting the number of metacystic amoebae after the induction of excystation, was inhibited by PKC inhibitors, staurosporine, chelerythrine chloride and calphostin C, in a concentration-dependent manner during incubation compared to the controls. As cyst viability was not affected by these inhibitors, reduced excystation was not due to their direct toxic effects on cysts. Metacystic development, when determined by the number of nuclei in amoeba, was delayed by these PKC inhibitors, because the percentage of 1-nucleate amoebae was lower than in controls at day 3 of incubation. Wortmannin, a potent inhibitor of PI3K, also inhibited excystation and metacystic development of *E. invadens* in a concentration-dependent manner compared to the controls. These results indicate that signaling through PKC and PI3K contributes to the excystation and metacystic development of *E. invadens*.

14C-09) POSTTRANSLATIONAL LIPID MODIFICATION OF RAB PROTEINS BY A PROTEIN GERANYLGERANYLTRANSFERASE TYPE II FROM *ENTAMOEBA HISTOLYTICA*

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The small GTPase Rab proteins function as a molecular switch of intracellular vesicular transport. They need to be posttranslatinally geranylgeranylated by a protein geranylgeranyltransferase type II (GGT-II) and also to be associated with a Rab escort protein (REP) to attach the membrane of intracellular transport vesicles and function. To clarify biochemical properties, we cloned GGT-II and REP from *Entamoeba histolytica* (*Eh*) and characterized the recombinant proteins. Alpha and beta subunits of *Eh*GGT-II and *Eh*REP, consisting of 317, 315 and 480 amino acids, had the conserved domains and showed 14-34, 42-49 and 18-23% identity with those of other organisms, respectively. Also, *Eh*GGT-II and *Eh*REP were phylogenetically independent of those of other organisms. Recombinant *Eh*GGT-II, which was purified as a heterodimer of two subunits, showed enzymic activity only in the presence of *Eh*REP when assayedusing *Eh*Rab5 as a protein substrate. There was difference in substrate activity among *Eh*Rab proteins. *Eh*GGT-II showed difference in substrate specificity compared to rat GGT-II. Further study will be done to evaluate the biological significance in difference between *E. histolytica* and mammalian GGT-II and REP and the possibility of the enzyme as a drug target against amebiasis.

Workshop C-2

14C-10) ARTESUNATE-AMODIAQUINE COMBINATION THERAPY IN UTAN, SUMBAWA, INDONESIA

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In the malaria control project that was implemented in Utan area of Sumbawa island from November 2002 to October 2004 under JICA partnership program, we found high prevalence of chloroquine resistant *Plasmodium falciparum* (*P. f.*) there. We requested the central government to introduce a new drug combination to this area, and got the permission to make the trial of Artesunate-Amodiaquine combination therapy. We received the drug combinations for 50 adults from the ministry of health, Indonesia. The teams for case detection and treatment were the same as those during the control project. They visited subvillages in the area, detected *P. f.* patients using ICT Malaria *P. f. / P. v.* diagnostic kit from clinically suspected malaria cases, and administered the new combination drugs to them after obtaining their informed consent. The efficacy of the drugs was examined by the follow-up study for 28 days. Complete cure was obtained in 60% patients after two days of treatment, 95% after 7 days and 100% after 14 days. No serious side-effects were seen during the first three days of treatment when the teams monitored. This combination was effective to asexual stage of parasites but not to matured sexual stage of parasites (gametocytes), which remained in blood for several days after disappearance of asexual forms but much shorter compared with remaining periods of gametocytes after chloroquine treatment. These results supported the alteration of the old drugs to the new combination.

14C-11) NEW ANTIMALARIAL ENDOPEROXIDE MECHANISM OF ACTION AND DEVELOPMENT OF RESISTANCE USING *PLASMODIUM FALCIPARUM, IN VITRO*

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Resistance to antimalarial drugs is increasing nearly everywhere in the tropical world, confounding global attempts to Roll Back Malaria. To combat the further spread of resistance, it is generally accepted that there is an immediate need for new effective antimalaria drugs with adequate knowledge of drug resistance mechanism. We developed about 5000 new antimalarial candidates and among these new antimalarial compounds we selected the most effective endoperoxide, N-89. N-89 is a effective antimalarial drug which showed high activity and selectivity. In this study we describe antimalarial activity of N-89 and cloning technique under drug pressure to get the double benefits of obtaining pure homogenous and resistant clone. We obtained Plasmodium falciparum clones resistant to a novel drug (N-89) with four folds increase in EC_{50} value and afford daily drug pressure concentration 2×10^{-6} M. Cross resistance to other antimalarial drugs was also tested. No cross resistance was observed to other structurally related (artemisinin) and structurally unrelated (quinine, chloroquine and mefloquine) antimalarial drugs. These parasite clones provide useful material for investigating possible drug resistance mechanism. We are currently using these parasite clones in proteome analysis, which enable us to define specific proteins related to the action of N-89 drug.

14C-12) NEW ANTIMALARIAL DRUG DEVELOPMENT －ANTIMALARIAL ACTIVITY AND PHARMACOKINETICS OF ENDOPEROXIDE－

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Malaria is parasitic disease caused by protozoan of the parasite Plasmodium. Currently more than 1 million people die of malaria each year. Unfortunately, the situation is getting worse with the emergence of multi-drug resistant Plasmodium species. Under the current circumstances without effective vaccine, it is very important project to develop new antimalarial drugs that can overcome the drug resistance. By the study of new antimalarial drug, we develop N-89 [1, 2, 6, 7-tetraoxaspiro (7, 11)- nonadecane] to identify potent antimalarial compound, which have cyclic peroxide formation like existing antimalarial drug, artemisinin. We examined the administration route which can be able to use in a coma of severe malaria case, administration schedule to effect a complete cure, and we also examined pharmacokinetics of N-89 by LC-MS. In an attempt to clinical use of N -89, we administered N-89 twice only first day and once daily for two consecutive days [75mg/kg/day, i.v.] when the parasite infection rate was 1%, and observed time-course changes in the infection rate. The parasite began to decrease 16 hours after the drug administration. The course was monitored for two months, and all five mice in the N-89 treatment group were completely cured. For the pharmacokinetics studies, blood samples were obtained sequentially after N-89was administrated to rats or mouse by the intravenous and oral routes. Concentrations of N-89 in plasma were determined by LC-MS after the pretreatment of acetonitrile solution. During single i.v. administration [30 mg/kg] the plasma concentration level of N-89 was decreased rapidly depend on concentration of N-89. This pattern correspond to 2 compartment model, it means N-89 distribute in tissue immediately and then excrete into the blood slowly. Tmax time is 0.5 [i.v.] and these results were same as we found in oral administration of N-89. We are now investigating the pharmacokinetics, antiamlarial action and general toxicity of N-89 to establish an appropriate administration method. In the conference, the current status of the development of novel antimalarial drugs is introduced.

14C-13) A CONSIDERATION TO MECHANISM OF ANTI-MALARIAL DRUG ACTION AND DRUG RESISTANCE CONSTRUCTION

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The world-wide-sprending drug-resistant malaria is a serious obstacle for Roll-Back-Program by WHO. We have investigated the reduction of drug-resistance of malaria by DSP (Dibenzosuberyl piperazine derivatives) to overcome these drug-resistance-problem, which would inhibit thiol-transporters such as MRP1. We have now found new effcts by DSP, anti-malaria effects and qunine-resitance-reducing effcts. Anti-malaria effect on BALB/c mice inoculated with chloroquin-sensitive P.chabaudi at dose of 5x10exp6, and resistance-reducing effect on BALB/c mice inoculated with chloroquin-resistant P.chabaudi at dose of 5x10exp6 was investigated. We revealed that DSP at dose of 20mg/Kg shows antimalarial effect. And chloroquin-resistant P. chabaudi had not only chloroquin-resistance but also quinine-resistance. DSP reduced both drug-resistance. It means DSP would be able to reduce multi-drug resistance of malaria.

14C-14) ANALYSIS OF MUTATIONS IN CYTOCHROME *b* GENE OF PLASMODIUM FALCIPARUM ISOLATES IN THAI-MYANMAR BORDER

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The combination of atovaquone and proguanil (Malarone™) has been established as a drug of choice to prevent and treat multi-drug resistant *Plasmodium* (*P.*) *falciparum* malaria in travelers. However several cases of resistance against Malarone™ have already been reported in some parts of Africa, and many of the cases are supposed to be associated with mutations at the codon 268 of cytochrome *b* gene in mitochondria of *P. falciparum*. Atovaquone is supposed to act on cytochrome *bc1* complex as a competitor of ubiquinol, inhibits electron transport in mitochondrial inner membrane and leads the parasite to death. Mutations around atovaquone-binding site in cytochrome *b* are supposed to cause atovaquone resistance. The objective of this study is to estimate effectiveness of Malarone™ on treatment, and prophylaxis for the travelers to Thai-Myanmar border where multi-drug resistant malaria is highly endemic.

Seventy *P. falciparum* samples taken from patients from Thai-Myanmar border were sequenced to detect mutations around the codon 268. Additionally other 4 codons in atovaquone-binding domain 272, 275, 280, 284, which were supposed to be related to atovaquone resistance, were also sequenced. All the 70 samples showed no mutations at the codon 268 of cytochrome *b* gene. Sixty-one cases were successfully sequenced for the other codons 272, 275, 280, 284, and they had no mutations.

In Asian countries, even in the multi-drug resistant areas in the great Mekong region, no case of Malarone™ resistance has been reported clinically or genetically yet. The more the usefulness of Malarone™ increases for both treatment and prophylaxis, the wider the drug-resistance against Malarone™ may spread in the region. Though the total number of investigated samples is not so large, we may conclude from these findings that Malarone™ should be recommended for prophylaxis and treatment of malaria in Mekong region by now.

14C-15) SCREENING FOR G6PD DEFICIENCY BY WST-8 METHOD (2): REACTIVITY OF BLOOD-SPOTTED FILTERS COLLECTED IN MALARIA ENDEMIC COUNTRIES

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WST-8 method is a simple and rapid G6PD-deficiency screening method which can be used under field conditions. This method is expected to be particularly useful for the on-site detection of partial G6PD-deficiency. Our recent laboratory evaluation revealed that not only whole blood but also blood-spotted filters are suitable for the WST-8 method. In the present study, blood-spotted samples collected in the fields were subjected to WST-8 method and the results were compared with those of *G6PD* gene analysis. A total of 680 samples collected in the field surveys conducted in Vietnam, Cambodia, Myanmar, and Indonesia, during 2003 and 2004, were brought back to our laboratory and subjected to the WST-8 filter method. Furthermore, 59 venous blood samples were obtained from those who had been judged as G6 PD-deficiency by the on-site WST-8test and agreed to give additional blood for *G6PD* gene analysis. Among 680 samples, 49 (7.2%) were judged as highly deficient (HD), and 55 (8.1%) were partially deficient (PD). Among 59 samples analyzed for *G6PD* mutation, 4 were mutation homozygote (3 were HD and1was PD by WST-8 test), 30 were hemizygote (28 HD and 2 PD), and 19 were heterozygote (3 HD, 14 PD, and 2 cases of slightly deficient), suggesting that G6 PD activity obtained by the WST-8 method correlates nearly with the genotype of *G6PD* mutation. On the other hand,

there were 49 cases judged as G6PD-deficiency (12 HD and 37 PD) by the WST-8 filter method, although their *G6PD* mutation analysis had not been made. Even when we consider those who had not agreed additional blood taking or cases of young children, a significant number in the 53 cases might have been overlooked by the on-site G6PD test. In order to establish efficient malaria control programs with using gametocytocidal drugs such as primaquine, it is essential to improve the accuracy of the on-site G6PD test. Therefore, we need to optimize the conditions of WST-8 method by both field- and laboratory-based studies.

Workshop D-1

14D-01) DISTILLING CLUSTERS FROM THE STATISTICS OF DENGUE IN VIETNAM USING A KRIGING INTERPOLATION APPROACH

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A number of visualizing techniques for disease clustering have been proposed including statistical and mathematical modeling approach. The statistical modeling approaches grasp an epidemic trend more effectively than mathematical one especially when large geographic variation was observed in epidemic data. Amongst such statistical models, kriging is the most suitable theory for geographic cluster observation because it requires fewer arbitrary parameters. Repeated outbreaks of dengue fever is a serious problem in Vietnam. The objective in present study is to distill clusters of dengue fever with application of kriging spatial interpolation. Vietnam disease statistic provided the number of clinic case of dengue fever by province from 1999 to 2003 with demographic data. Annual morbidity rates of dengue fever by province were calculated, each of which was linked to a geometric centroid of province. Estimates for spatial interpolation were computed with normal kriging model derived from the centroids with morbidity rate. On the map spatially interpolated, clusters were especially observed in the southern areas around Tay Ninh Province and the central area around Gia Lai Province in 1999. The trend in 2000 is almost same as 1999 except disappeared smaller clusters. Larger outbreak struck Vietnam in 2001. The south cluster moved slightly toward the ocean side, and the central cluster shifted slightly to the north. In 2002, the south cluster changed the position more closer to ocean side. And in 2003, the south cluster reached the seashore in Ben Tre Province and the central cluster shifted more to north. Spatial interpolation from centroid of province is essentially different from mapping colored with province boundaries; it means the interpolation ignores topographic or social boundaries. Conversely, it rather preferable to understanding the global trend of dengue epidemics in this study. The reason of moving cluster is yet to be clarified. It possibly provides a clue to build a predictive model of dengue outbreaks. This study was supported by JSPS Core University Program.

14D-02) MOLECULAR EPIDEMIOLOGY OF DENGUE VIRUS SEROTYPE 2 IN THE PHILIPPINES

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Background

Dengue fever has been occurring endemically in many areas of the Philippines particularly in Metro Manila and other urban localities of the country. Of the four serotypes, DENV 2 has been consistently detected in outbreaks/epidemics from 1995 to 2002. Only a limited data on the molecular epidemiology of DENV 2 in this country, however, is available. This study aims to determine the genetic variability of DENV 2 circulating locally and identify possible associations between virus genetic subtype and severity of clinical presentation.

Materials and Methods

A total of 41 strains from Dengue fever (DF), Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS) patients between 1995 and 2002 were isolated. The pre-Membrane (prM) and envelope (E) genes from these isolates were sequenced and aligned for comparison. The envelope sequence data were compared with 38 DENV 2 E gene sequences from different geographic areas including 13 previously isolated Philippine strains available in Gen-

Bank.

Results

Phylogenetic analysis revealed that two distinct genotypes of dengue 2 virus are currently circulating in the Philippines. Asian 2 genotype was constituted mostly of earlier isolates (48.0%) obtained from 1995 to 2002. Fifty-two percent of local isolates on the other hand were of Cosmopolitan genotype the majority of which were collected from 1999 to 2002. None of the amino acid changes were consistent between DF and DHF/DSS samples and thus could not be correlated with disease outcome.

Conclusion

The phylogenetic data suggests that DENV 2 strains circulating in the Philippines are mainly of the Cosmopolitan genotype, displacing Asian 2 genotype over a short period of time since its introduction in 1998. Although no consistent sequence differences were observed to distinguish isolates that may cause more severe disease, increased pathogenicity may be caused by nucleotide changes in the viral genome other than the prM and envelope regions.

Collaborators

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14D-03) GENETIC ANALYSIS FOR SUSCEPTIBLE GENE TO DENGUE HEMORRHAGIC FEVER IN VIETNAM

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Dengue fever is getting a serious public health problem in many regions of the world, Almost 1 %of the patients with Dengue Fever (DF) develop Dengue Hemorrhagic Fever (DHF), or Dengue Shock syndrome (DSS). Two factors are proposed to be important to produce DHF / DSS. One is viral virulence and the other is host genetic factor. In this study, we made an experimental design to identify the host gene (s) contributing to the development of DHF / DSS in Vietnamese by case control study. The patients with DHF or DSS were clinically diagnosed by WHO criteria, and their peripheral blood samples were collected at the Center for Preventive Medicine, Vinh Long Province (VL), and the Pediatric Hospital No. 2, Ho Chi Minh City (ND2) in 2002 to 2003. The patients age ranged between 10 months and 15 years. 200 age and sex matched control samples were collected in Vinh Long. The number of the patients with DHF cases was 20 from VL, 121 from ND2, and that of the patients with DSS was 172 from VL, 159 from ND. DNA was extracted from each blood sample, then HLA class I (HLA-A, B), class II (DRB1) and TNF-αpromoter SNPs typing were performed. There was no significant difference in HLA-A, HLA-B and TNF-αpromoter SNPs alleles. However, HLA-DRB1*0901 was significantly decrease in DSS. The DRB1*0901 allele might directly contribute to resistance to DSS or might be a genetic marker that has strong linkage disequilibrium with some resistant gene.

14D-04) SEROEPIDEMIOLOGICAL STUDY ON HBV, HCV AND HIV INFECTIONS AMONG VOLUNTARY BLOOD DONORS IN LAO PDR

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[INTRODUCTION] Southeast Asia is a highly endemic area of HBV infection and also HCV infection in some regions. Not only HBV and HCV infections but also HIV infection is still raging in this area. However there are few epidemiological reports of these blood-borne diseases from Lao PDR. [MATERIALS AND METHODS] The total number of 4,739 serum samples from the first time voluntary blood donors (2003-2004, 17-64 years old; male: 3,400, female: 1,339) in Vientiane area was examined for HBs-Ag, anti-HCV and anti-HIV1/2. [RESULTS] 1) HBs-Ag positive rates by age; 17-20 years old: 9.1% (male: 10.6, femal: 6.1%), 21-30 years old: 9.0% (male: 10.0, female: 5.4%), 31-40 years old: 5.7% (male: 6.1, female: 4.2%), 41-50 years old: 2.1% (male: 0.0, female: 10.3%), 51 years old and over: 9.4% (male: 4.2, female: 25.0%) and total positive rate was 8.6%. 2) Anti-HCV positive rates by age; 17-20 years old: 0.6% (male: 0.6, female: 0.7%), 21-30 years old: 1.2% (male: 1.2, female: 1.2%), 31-40 years old: 2.3% (male: 2.5, female: 1.4%), 41-50 years old: 2.1% (male: 1.7, female: 3.4%), 51 years old and over: 3.7% (male: 4.2, female: 0.0%) and total positive rate was 1.0%. 3) Anti-HIV1/2 positive rate. Only 2 cases of male, 28 and 42 years old respectively, showed positive and total positive rate was 0.04%. [CONCLUSION] Our findings suggest that Vientiane area of Lao PDR belongs to a high prevalence region group of HBV infection by WHO classification and HBV infection is predominant more than HCV infection at the present stage. However due to the biological characteristics of HCV, a high tendency to progress to chronic diseases and hepatocellular carcinoma, HCV infection will become a more important medical problem in the near future. On HIV infection, although the positive rate is very low at present, it is concerned that the patients with HIV infection will rise in number with the continuing increase of people exchange among the neighbouring countries.

14D-05) INTER-CRF RECOMBINANTS (ICRS): DISCOVERY OF NEW CLASS OF HIV-1 RECOMBINANTS AND ITS EPIDEMIOLOGICAL IMPLICATIONS

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Background: Diverse forms of HIV-1 recombinants appears to be arising continually in previously identified geographical recombination hotspots found in Asia, including Yunnan Province of China and Myanmar. We carried out the molecular epidemiological investigation to monitor the genetic variability of HIV-1 strains and studied the detailed structural characteristics of HIV-1 recombinants emerging in these areas.
Methods: We determined near full-length nucleotide sequences of HIV-1 recombinants found in Myanmar and Yunnan Province. Recombination breakpoint analyses, including, bootscanning, informative site and subregion tree analyses, were performed to define their recombinant structure, and bootstrap values were used to confirm the subtype assignments.
Results: We identified approximately 12% of HIV-1 strains found among IDUs in southeastern Yunnan are the diverse forms of inter-CRF recombinants between previously estab-

lished CRF07_BC and CRF08_BC (n=5). Similarly, continued monitoring of HIV-1 strains in Myanmar identified the second class of HIV-1 inter-CRF recombinants comprised of CRF07_BC and CRF01_AE (n=3)among24recent HIV-1 isolates in Yangon (in 2002-2004).
Conclusions: Mixing of different lineages of HIV-1 strains in highly-exposed population leads to the evolution of new forms of HIV-1 recombinants and even the second-generation recombinants between previously established CRFs. In the present study, we identified two novel classes of inter-CRF recombinants (ICR) between CRF07_BC and CRF08_BC in Yunnan Province (China) and between CRF 07_BC and CRF01_AE in Yangon (Myanmar). This suggests the dynamic relationship of the epidemic in Asia. We propose to designate these new recombinants as ICR01_ 0708 and ICR02_0701.

14D-06) POSSIBLE RISK OF SALMONELLA INFECTION FROM MARKET FOODS IN VIENTIANE CAPITAL, LAO PDR

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In Vientiane Capital of Lao PDR, occurrences of frequent cross contamination by food-borne bacteria species of Vibrio and Salmonella was pointed out at the last in Kitakyushu (Midorikawa et al., 2003). Salmonellosis is one of the commonest but serious health problems in the developing countries. Therefore, to clarify the actual situation of Salmonella contamination at some food markets in Vientiane is still important. The study was conducted around 10 days both in September (the rainy season) and in December (the dry season) in 2004. The bacteria were examined from the surface of domestic animal and fish meats, some vegetables and cookers available from the markets. A new method developed by us (Midorikawa et al. 2004) was also employed to detect Salmonella, in addition to classical Invic screening. Four Salmonella species were recovered from 41 foods samples (9.8%) and 6 Salmonella species were also recovered from stool samples of 39 healthy dwellers (15%) in the rainy season. Salmonella contamination in food samples was lower in the dry season. Salmonella sero-typing resulted in some common species between the foods and the stools samples. The genomic analyses of these strains are in progress. The risk of Salmonella infection from market foods will be discussed herein.

14D-07) PREVALENCE OF RESPIRATORY INFECTION CAUSED BY STREPTOCOCCUS PNEUMONIAE AND HAEMOPHILUS INFLUENZAE IN THE CAMPS OF TSUNAMI AFFECTED AREA IN SRI LANKA

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Our objective was to investigate the status of acute respiratory tract infections caused by Haemophilus influenzae and Streptococcus pneumoniae in tsunami disaster evacuation camps. Nasopharyngeal swabs (NP) of 324 internally displaced persons (IDP) in 3 different tsunami disaster evacuation camps of Sri Lanka were collected between March 18 and 20, 2005 and analyzed for MIC, beta-lactamase production, serotypes, PCR and pulsed-field gel electrophoresis (PFGE). The prevalence of at least one of the following respiratory symptoms; snivel, sore throat, cough and sputum were 84%, 70.5% and 64.7% in each camp. Twenty-one H. influenzae from IDP and 25 S. pneu-

moniae from 22IDP were isolated from the NP. All H. influenzae isolates were nontypeable and 5were beta-lactamase producing. Seventeen pneumococci were susceptible, 5 showed intermediate resistance and 3 were fully resistant to penicillin G. molecular typing by PFGE showed the 21 H. influenzae had 13 patterns and 25 pneumococcal strains had 16patterns. Each of the 2 different patterns of H. influenzae were detected in 2 or 3 IDP in camps 1 and 3. Different PFGE patterns of serotype 3 and 22A pneumococci were detected in 2 or 3 IDP in camp 1, and those with serotype 9 A, 10A and 11A were detected in 2 IDP in camp 3. Our data indicate acute respiratory tract infections caused by various types of H. influenzae and S. pneumoniae appear to have been prevalent, some of which were transmitted from person to person in tsunami disaster evacuation camps.

14D-08) PHENOLYC GLYCOLOPID-1 (PGL-1) IN TISSUES INFECTED BY *MYCOBACTERIUM ULCERANS*

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Mycobacterium ulcerans is the causal agent of Buruli ulcer, a disease recently highly prevalent in some part of Africa. The world wide endemic distribution of the disease is being revised due to change in investigative strategies for its detection. Ulcers is the most advanced lesion of the disease, although other forms like papules, plaques, edema and nodules exist. The causal agent of Buruili ulcer, *Mycobacterium ulcerans* is close to *Mycobacterium tuberculosis* and *Mycobacterium leprae*. In this work, we have investigated the presence of Phenolyc Glycolipid-1 (PGL-1), a carbohydrate - based antigen, generally known as specific to Mycobacterium Leprae in tissue infected with *Mycobacterium ulcerans* . The potential use of this antigen for early detection of the disease, a key factor to preventing progress to aggravated stages, has prompted this work.Materials and MethodsSkin flaps were surgically obtained from 30 patients clinically diagnosed as Buruli ulcerat the AGROYESUM HOSPITAL in ASHANTI COUNTRY OF GHANA where BuruliUlcer is endemic.

Results

Clinical form	Patients	Acid fast bacilli Stain (+)	PGL-1 (+) by immunostain
Plaques	3	1	1
Nodules	10	5	5
Ulcerated nodules	1	0	0
Deep ulcer bed	7	4	4
Healing ulcer	9	2	2

Acid fast bacilli stains: Fite-Faraco & Harada stains./ PGL-1: Phenolyc glycolipid- 1CONSIDERATIONS 1/The above results suggest that PGL-1 may not be specific to one member of the mycobacterium genus and that mycobacterium ulcerans wall probably expressthe antigen. 2/What role exactly Phenolyc glycolipids play in the pathogenesis of this ulcerative disease should be further investigated.

Workshop D-2

14D-09) LATENT INFECTION OF MALARIA PARASITES IN SCHOOL CHILDREN LIVING IN THE ENDEMIC ARIA IN VIETNAM

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Detection of asymptomatic carriers of parasites and complete treatment of them is one of essential measures in malaria control, because they are potentially healthy gametocyte carriers. We have been noticing that even school children have high titer of anti-parasite antibodies an that they harbor malaria parasites without any malaria symptoms in our study site in Vietnam. Furthermore, there were tendency that when a school child was diagnosed as malaria by microscopy, its brothers and sisters were also infected with parasites. These imply that there should be parasites carriers in the vicinity of infected people and that microscopic negative should not be true negative. We compared PCR diagnosis with microscopic diagnosis on the blood samples from the endemic area to confirm whether microscopic examination grasps real situation of malaria infection. After obtaining a written informed consent of the parents we collected blood from school children in Phu Thuan, Binh Phuoc Province one time a week over five weeks in a rainy season in 2003. Slide-positive children with P.f at week 0 and at the first time during the study period were regularly treated with artesunate according to the policy of Vietnam. Vivax malaria was regularly treated with chloroquine and primaquine. When school children turned to be slide-positive again, they were given CV8 according to the policy. The prevalence by microscopy was 36% by microscopy and that by PCR was 61% against malaria infection. That was 27 and 47% against falciparum malaria. P.v, P.o, and P.m were more fluently detected by PCR than by microscopy. These infections were detected as mixed infection with other species. When PCR diagnosis was a golden standard, specificity of microscopy was 100%. Sensitivity of microscopy, however, 60%against malaria, 50% against falciparum malaria, and occasionally reduced to be 10%. In several cases we observed that parasites remained one week after treatment by PCR. On the other hand, we noticed that parasites disappeared and changed to other species without any treatment. The results suggest that parasite number should fluctuate sub-microscopic level and that PCR negative should not be true negative although it sensitivity was higher than that of microscopy.

14D-10) SCHOOL BASED MALARIA EDUCATION IN MEKONG SUB-REGION

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Malaria education in a primary school has already been recognized one of the health education strategies in malaria control among Mekong countries. Asian center of international parasite control (ACIPAC), which was conducted by Thailand and Japan technical cooperation, has developed the concept of the strategy and the field model. The concept of school based malaria education was developed on the basis of health promoting school, which has been emphasized by WHO. Especially, cooperation between school and community was strengthened in the concept. Teachers in the model schools in Thailand conduct the health education using by participatory learning action approach to promote schoolchildren to play important roles as messengers for malaria prevention in the community. ACI-

PAC has introduced the concept on the international training course and several international and domestic conferences in the Mekong sub-region from 2002. In Thailand, the school based malaria education in the elementary school has been conducted in not only ACIPAC model area but also several provinces located in Thai- Myanmar border, where malaria is still public health problems. In Cambodia, the malaria education has been started as a national program supported by Global fund. ACIPAC trainees have developed the proposal. In Myanmar, malaria education has already included one of topic on the curriculum in the elementary school. Small scale pilot project supported by ACIPAC was strengthened this program including in participatory learning approach. The policy maker in the government was recognized the approach in the malaria control and school health. Moreover, the importance of the intra-sector cooperation in the malaria education was recognized as a global strategy among the member nation in World Health Assembly, 2005.

14D-11) PREVALENT DISTRIBUTION OF KOBE-SSURDNA-TYPE-BABESIA MICROTI IN RODENTS IN THE SOUTHERN PART OF MAINLAND OF CHINA AS WELL AS TAIWAN

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Most cases of human babesiosis have been reported in the United States of America (USA) and in Europe. Cases have been mainly caused by *Babesia microti*, a rodent babesia, and *Babesia divergens*, a bovine babesia, in the USA and Europe, respectively. In Asia, a few cases of human babesiosis were reported in Mainland of China (Yunnan, Inner Mongolia and Zhejiang), Taiwan (Chiayi) and Japan (Hyogo). The etiological parasites of all cases in Mainland of China have not been clearly identified. The etiological babesia of the Taiwanese case was only shown to be serologically related to *B. microti*. The Japanese case was caused by blood transfusion from an asymptomatic donor who resided in Awaji Island, Hyogo. The SSUrDNA sequence of the etiological babesia (Kobe type) was most homologous but not identical to that of *B. microti* originated from endemic regions of the USA (US type).

As we previously reported, Otsu type-*B. microti* (another SSUrDNA-type of Japanese *B. microti*) is widely distributed in rodents in Japan, while Kobe type-*B. microti* seems to be localized in a few certain regions, so far in Awaji Island and in Aomori Prefecture. US type-*B. microti* was found in Sapporo, Hokkaido. On the other hand, in Taiwan, Kobe type-*B. microti* was identified in Kaosiung and Nantour. Taiwanese Kobe type-*B. microti* was differentiated from Japanese Kobe type-*B. microti* by the internal transcribed spacer 1 and 2 (ITS1/ITS2)sequences.

We started the survey in the southern part of Mainland of China (Fujian and Zhejiang) in 2005. *B. microti* was detected in 14 (*Niviventer confucianus* 13; *Apodemus agrarius* 1) of 31 rodents by thin blood smear observation and/or PCR. The SSUrDNA sequences of *B. microti* parasites in 13 rodents were completely identical to Kobe type-SSUrDNA. The ITS1/ITS2 sequences of the 13 parasites were more similar to those of Taiwanese Kobe type-*B. microti* than those of Japanese Kobe type-*B. microti*. The SSUrDNA and ITS1/ITS2 sequences of the parasite in the rest one *N. confucianus* rodent were different only by two nucleotides (one in the SSUrDNA sequence and one in the ITS1/ITS2 sequences) from those of Japanese Kobe type-*B. microti*.

It was demonstrated for the first time that Kobe type-*B. microti* was widely distributed from the southern part of Mainland of China, Taiwan to Japan, where Asian human babesiosis cases so far emerged. The finding suggests that Kobe type-*B. microti* may play an important role in emergence of human babesiosis in Asia.

14D-12) IDENTIFICATION OF CAUSATIVE PARASITES OF LEISHMANIASIS IN PAKISTAN BY CHYTOCHROME *b* GENE ANALYSIS

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Pakistan, located in Middle-East Asia, is one of endemic areas of Leishmaniasis. The causative parasites of Leishmaniasis in Middle-East Asia reportedly include *L. (L.) major* and *L. (L.) tropica.* During the three-year period from January 2003 to December 2004, we diagnosed and treated patients with Leishmaniasis who lived in Pakistan. We identified the causative *Leishmania* parasites by cytochrome *b* gene analysis using biopsy specimens and cultured parasites collected from the patients.

Subjects and methods: Sixty patients (40 males and 20 females) with Leishmaniasis in Pakistan were diagnosed by clinical symptoms, histological findings, Giemsa staining, separate culture, and other methods. The ages of the patients ranged from 5 months to 50 years with the average of 20.7 years. The methods to identify the causative parasites were as follows: 1) extraction of DNA from the biopsy specimens and/or cultured parasites; 2) PCR with consensus primers of *Leishmania* cytochrome *b* gene; 3) direct sequencing of the amplified PCR products to determine the base sequences for identification of the parasites.

Results: There were 46 cases of *L. (L.) major* and 13 cases of *L. (L.) tropica* and one unknown case. 45 cases of *L. (L.) major* were found in Larkana city located in Indus Valley and in the area surrounding Sukkur city. 12 cases of *L. (L.) tropica* and one case of *L. (L.) major* were found in Quetta city, a mountainous region near Afghanistan.

Discussion: The number of cases of Leishmaniasis in the vicinity of Larkana city increased rapidly from 16 in 1996 to 300 in 2001. This provoked a public health problem (Bhutto AM et al, Int J Dermatol, 42: 543, 2003). However, no reports have been identified the causative parasites in this area. The present study revealed that most of the patients with *L. (L) major* were found in Indus Valley, and those with *L. (L.) tropica* were distributed in a mountainous region near Quetta city.

14D-13) PREVALENCE OF *LEISHMANIA DONOVANI* SPECIFIC URINARY ANTIBODY IN A COMMUNITY IN BANGLADESH

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Visceral leishmaniasis (VL), after passing 100 years from its clinical descriptions by Leishman and Donovan in 1903, the status of the disease has been upgraded to “most neglected” disease from its traditional position as simply a

"neglected" disease. Approximately 90% of the 500,000 estimated new annual cases of VL occur in rural areas of Bangladesh, India, Nepal, Sudan, and Brazil. Very few studies have been reported on prevalence of VL in Bangladesh. Recently, we have developed methods to detect *Leishmania* antigen specific antibodies in urine samples: ELISA using acetone treated antigen (urine ELISA) and recombinant kinesin-related protein with a molecular weight of 42-kDa (rKRP42 urine ELISA) for the diagnosis of VL, which showed almost the same sensitivity and specificity as with serum samples. We have applied these methods in a village named Nobai Bot Tala with a population of 527, in Godagari Thana, Rajshahi district, to determine the prevalence of *L. donovani* specific antibody among the populations. During our1st visit in March 2005, we registered 302 volunteers in our study and collected urine samples after getting their informed consent. We got 14.6% (44 positives/ 302) *L. donovani* specific antibody positive among the volunteers, of which 45.5% (20/44) male and 54.5% (24/44) female. Among the 44 positives 9 were previously treated for VL, and the rest had no past VL history. All the cases who were clinically suspected and positive by our test (s) were advised to visit to Rajshahi Medical College Hospital (RMCH) for better clinical evaluation and treatment. In our 2nd visit in July 2005, we collected 454 urine and serum samples from the previously and newly registered volunteers. We will discuss the occurrence of clinical cases among the antibody positives, changes of antibody titer among treated cases, and also the incidence of *L. donovani* specific antibody among the study populations.

14D-14) EPIDEMIOLOGICAL STUDIES ON HUMAN CUTANEOUS LEISHMANIASIS IN SRI LANKA

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Cutaneous leishmaniasis cases have recently increased throughout Sri Lanka since the first case was reported in 1992. Epidemiology of leishmaniasis in this country however has still been unclear. An epidemiological research has been performed since 2003 in Anuradhapura, Kurunegala, and Matale district in Sri Lanka to identify pathogenic species and investigate clinical features. Skin aspirates from 57 clinically suspected cutaneous leishmaniasis patients were cultured in NNN medium, and *Leishmania* promastigotes were detected in culture form 20 out of 57 patients. Using Sri Lankan isolated parasites, the nucleotide sequences of a region of the actin-encoding gene, which is highly conserved among eukaryotes, was analyzed. The actin-encoding gene from the Sri Lankan isolate was compared with those from the reference strains of *L. major* and *L. donovani*. Sri Lankan isolate differed by only 1 bp from *L. donovani* while Sri Lankan isolate and *L. major* differed by 34 bp. The PCR products of the mini-exon gene, which is unique in the genus *Leishmania*, were compared with those of reference strains of *L. donovani*, *L. major*, *L. tropica* and *L. amazonesis*. Interestingly, Sri Lankan isolate yielded two products of different sizes which is same products pattern with *L. donovani*, which is the principal pathogenic species of visceral leishmaniasis. The skin lesions of patients from whom *Leishmania* parasites were detected occurred in exposed areas like the face, arms, and legs, and were 5-20 mm in diameter. Some lesions lasted 4 to 10 months as blister in appearance. All patients were negative in Kalazar detect dipstick for visceral leishmaniasis (InBios International Inc., Seattle, USA), which is antibody detection assay to rK39 antigen and highly sensitive for visceral leishmaniasis caused by parasite members of the *L. donovani* complex. ELISA using the same rK39 antigen showed that the optical density value of plasmas from 11 patients obtained in 2004 were low (0.30 ± 0.2) compared with positive control (3.06), although that of negative control (Japanese healthy volun-

teer) was 0.1±0.09. Those results suggest that human indigenous cutaneous leishmaniasis caused by the parasites belonging to *L. donovani* complex is endemic in Sri Lanka.

14D-15) NEEM OIL AS BIOLOGICAL CONTROL AGAINST PHELEBOTOMINE SANDFLY

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Objective: The study aims to evaluate the effect of neem oil against Phlebotomus argentipes.Methods: This study was conducted in a kala-azar endemic area of Mymensingh, Bangladesh. CDC miniature light traps were used for the baseline collection of sandflies from the dwelling houses. Traps were set at 17:00-18:00 hours and collected at 5:00-6:00 hours on the following day. A total of baseline 72 trappings was made. Among the baseline houses, 30 houses were selected on a basis of abundance of sandflies. Neem oil solution with detergent emulsifier was sprayed on the house wall in a concentration of 100 ml/m2. Control houses were sprayed with only detergent solution. Effects of neem oil on sandflies were evaluated by trappings on the 3rd and 7th days. Results: A total of 1,005 sandflies were collected from single night collection; 657 were males and 348 females from 98 screened houses. Neem oil with detergent was sprayed on 18 houses and 12 houses were only sprayed with detergent. Significant reduction in sandfly number was observed among neem oil sprayed houses compared to the control houses (76% and 41% reduction respectively). Conclusion: This study demonstrated the effect of neem oil solution application on wall for reducing the number of sandfly. Further study requires confirming the longer duration of the effect.

Workshop C-3

15C-01) PRELIMINARY STUDIES ON THE EFFECT OF T CELL- AND INFLAMMATORY CYTOKINES ON MUCIN-RELATED GENE EXPRESSION IN INTESTINAL EPITHELIAL CELLS

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Regulation mechanisms of the mucus production and secretion induced by intestinal nematode infection still remain to be elucidated. We examined the effect of sodium butyrate (NaB) and various cytokines (IL-4, IL-13, IL-17, IL-6, TNFα and IL-1β・ on gene expression of mucin- and glycosylation-related genes in rat small intestinal epithelial stem cell-derived cell line IEC-6.

[Method] Semi-confluent IEC-6 cells cultured in the internal wells of 24-well double chamber dishes with DMEM medium containing 5% FCS and 5μg/ml insulin at 5% CO2 atmosphere were used throughout the study. After adding NaB (final 1 mM) and incubating for 24 hours, cytokines were added and IEC-6 cells were further incubated for another 24 hours. cDNA was synthesized after collecting total RNA form IEC-6 cells, and real-time PCR was performed. Genes examined were mucin core peptide (MUC) 2, MUC5 AC, goblet cell specific peptide trefoil factor family (TFF) 3, resistin-like molecule (Relm) β, one of sialyltransferases, Siat4c, and one of sulfotransferases, 3ST1.

[Result] Addition of NaB in the culture medium resulted in marked upregulation of TFF3: 20-times higher than cultures without NaB. In cultures incubated with NaB and further added with Th2 cytokines IL-4 or IL-13, gene expression of Siat4c and 3ST1was markedly upregulated. Addition of pro -inflammatory cytokine IL-6 following NaB administration showed a mild upregulation of MUC2. Other cytokies, IL-17, TNFα or IL-1β showed no significant effect on gene expression of IEC-6 cells.

These results indicated that NaB stimulates IEC-6 cells to express TFF3, one of secretory molecules expressed in mature goblet cells. Th2 cytokines IL-4 and IL-13 might alter mucin- or membrane glycoprotein-glycosylation status by upregulating sialyl- and sulfo-transferases.

15C-02) MECHANISM OF MUCOSAL PROTECTION AGAINST NEMATODE INFECTION: ALTERED EXPRESSION OF GOBLET CELL- AND MUCIN GLYCOSYLATION-RELATED GENES IN THE INTESTINAL EPITHELIUM IN RAT

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Although mucus response is considered to play an important role of mucosal protection against damages incurred by pathogens, it has also been suggested to be responsible for the rejection of nematodes from the intestine.

To investigate whether there were alterations of the expression of goblet cell-and mucin glycosylation-related genes during nematode infection, epithelial cells were isolated from the small intestine of Brown Norway rats and mast-cell deficient Ws/Ws rats after *Nippostrongylus brasiliensis* infection, and gene expression levels of 3 types of mucin core peptides, 3 types of glycosyltransferases and 3 kinds of non-mucin peptides were determined by semi-quantitative reverse transcription (RT)-PCR.

Among the genes investigated, mucin core peptide (MUC) 2, trefoil factor family (TFF) 2, TFF3 and sialyltransferase (Siat) 4c were up-regulated as early as 2-4 days post-infection. Seven days post-infection, up-regulation of MUC3, MUC4, resistin-like molecule (Relm) β and 3O-sulfotransferase (3ST) 1 was observed, while 3ST2 expression levels increased after worms were expelled. This result shows that expression levels of each goblet cell-and mucin glycosylation-related genes altered differently along the

course of infection indicate progression of sequential qualitative changes in mucus properties after infection.

Similar alterations of gene expression were observed in Ws/Ws rats, suggesting that mast cells in the epithelium are not relevant to up-regulation of these genes.

15C-03) PROTECTIVE IMMUNITY AGAINST *H. NANA* ONCOSPHERES IS ESTABLISHED INDEPENDENT TO KNOWN APOPTOSIS REGULATORY MOLECULES

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Host's intestine is important on the host resistance to orally infectious parasites. However, immune system to intestinal parasites is yet unclear. Mice receiving a single oral inoculation of *Hymenolepis nana (H. nana)* eggs acquire a strong protective immunity and a challenge infection with eggs will be completely rejected by inhibiting larval growth in the intestinal villi. This strong resistance to re-infection is established on 24hours after immune infection. This acquired immunity is dependent on CD4 positive cells. We focused our studies on in vivo analysis of the role of apoptosis regulatory molecules in host defense mechanisms against *H. nana* re-infection in mice. Primary infection of *H. nana* was carried out by giving 1000 eggs on day 0. The mice were challenged orally with 1000 eggs on day 5 and killed 4 days later. The protective effect was assessed by counting the *cysticercoids* which had developed in the intestinal villi by day 9, 4 days after challenge. Monoclonal antibodies were intraperitoneal injected at 0.5mg on 2 hours before challenge infection. These antibodies are blocking monoclonal antibodies against mouse Fas L, TNF and CD40 L. Treatment of neither antibodies on protective immunity failed to suppress acquired resistance to *H. nana* re-infection. Fas knock out mice were carried out as above infection. In this knock out mice, protective immunity also failed to suppress acquired resistance. The present results suggest that protective immunity against *H. nana oncosphere* is established independent to known apoptosis regulatory molecules.

15C-04) SCHISTOSOMIASIS HAEMATOBIA: DIFFICULTY OF URINATION

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Hospital-based studies report that most patients infected with Schistosoma haematobium, present varying symptoms when they pass the urine. The present study was attempted to quantify the difficulty in micturition of school boys, aged from 9 to 16 yrs old, in an endemic area of schistosomiasis in Kenya. The boys were examined for the eggs in urine and for the bladder pathology. Among the boys who passed the eggs, 46 boys, 23 with bladder pathology and 23 without pathology, were then questioned on the difficulty in micturition by International Prostate Symptoms Score (IPSS) and by a questionnaire on dysuria. And they were examined for the voiding function by the portable uroflow meter. Since the difficulty in micturition may principally be due to the bladder pathology, the results of our studies were compared between boys with and without the pathology. The average of the grade of bladder pathology of 23 boys (WHO standard) was 2.6. There was no difference in intensity of infection between the boys with and without the pathology (61.2 and 58.6 eggs/ 10ml of urine). IPSS over 8 manifests the difficulty in micturition. The mean and SD of IPSS of boys with the bladder pathology was 15.4± 5.9 and those of boys without pathology was 12.7±9.4. The passing of urine is usually accompanied by burning and painful micturition. There was no difference in frequency of

dysuria between the boys with and without the pathology. Pain is felt over the suprapublic region and near the end of urination. Pain is characterized by the sense of a pricking or sharp and cutting pain. Uro-flow meter showed the significant difference in the voiding function between the boys with and without the pathology. T to Q max (sec) and Q max/ V void of the boys with the pathology were 7.4 and 1.97. The corresponding values of the boys without the pathology were 11.0 and 1.43. The results of uro-flow meter indicates that the boys with pathology urinate more powerfully or urgently than those without the pathology. The present study offered some clarification on the difficulty in micturition.

Workshop C-4

15C-05) USEFULNESS OF URINE-ELISA WHICH DETECTS FILARIA SPECIFIC IGG4: A SURVEY IN JIANXI, CHINA

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In China, lymphatic filariasis was widespread in 16 out of 36 provinces/autonomous regions/municipalities (P/A/M) in 1950s. Number of the patients was estimated to be 31 million. Following National Filariasis Control Program, the positive rate of the disease was decreased to less than 1% in all endemic areas by 1994. Then Ministry of Health declared 'basic elimination' of filariasis. By 2001, Ministry of Health declared 'true elimination' of filariasis in eight P/A/M where microfilaria positives had not been found for 10 years. For declaration of 'true elimination' in the rest eight P/A/M, huge number of night blood samples must be examined. Our survey in Zhejiang Province in 2002, where 2,800 residents were examined with a urine based ELISA for filarial antigen specific IgG4, suggested usefulness of the ELISA to assist the confirmation of 'true elimination'. In this survey, we examined 8,046 urine samples from students of 57 schools in Gaoan, Jiangxi Province using the urine based ELISA. Microfilaria (mf) positive rate in Gaoan was 4.5% before a filariasis control program launched in 1971. Mass drug administration by DEC salt was made in 1999. Microfilaria positives have not been detected since 2002. *Brugia pahangi* female antigens were used to detect filarial antigen specific IgG4 in the urine samples by ELISA. Among 8,046 urine samples examined, 8,016 (99.6%) were negative with the urine ELISA. Twenty-eight samples were positive but most of them showed low antibody titers. Students with the urine ELISA positives were examined in blood mf, blood antigen (by ICT) and urine based ELISA again; all tests showed negative results. As the filariasis control program progressed and number of symptomatic filariasis patients decreased, it become difficult of obtain collaboration of residents, especially for a night blood mf survey. The urine based ELISA uses urine samples collected at daytime and can examine a large number of samples in a short period. The urine based ELISA is a useful tool for evaluation of filariasis control program.

15C-06) INTESTINAL PARASITIC INFECTIONS IN SCHOOL CHILDREN IN A SUBURBAN AREA OF HANOI, VIETNAM

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An epidemiological study on intestinal parasitic infections among school children in a suburban area of Hanoi, Vietnam, was conducted. Of the 217 school children involved in this study, 166 (76%) were positive for at least one of nine species of parasite (six helminths and three protozoa). Among the helminth parasites, *Trichuris trichiura* (67%) was detected the most frequently followed by *Ascaris lumbricoides* (34%) and hookworm (3%). In the case of protozoan parasites, *Entamoeba coli* (8%) was the most frequently detected followed by *E. histolytica* (2%). No *Cryptosporidium parvum* or *Cyclospora* sp. were found. A questionnaire survey revealed that there was no positive relationship between parasite infection and the children's school records, educational background or parental income, which have been known to play a role.

15C-07) STUDY ON TRANSMISSION AND INFECTION OF SOIL-TRANSMITTED NEMATODE IN THE SUBURB OF HANOI, VIETNAM: CONTAMINATION OF WATER AND AIR WITH PARASITE EGGS

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We are carrying out an epidemiological study on a soil -transmitted helminth infection in a village located in the suburb of Hanoi, Vietnam. We have already reported that the soil, dust, vegetables, and fingers and nails were contaminated with parasite eggs. In the present study, we attempted to detect parasite eggs in water and air samples. In the study area, the well water was used for daily life, and rain water is also used in some households. The examination of water and air was conducted in the rainy season (June-August) and the dry season (December-February). Two litter water samples were collected from 29 households, two schools, two kindergartens, one restaurant, two ponds, one lake and 23 ditches. The examination showed that 13.8% of water samples from households and all water samples from ponds, lake and ditches were contaminated with parasite eggs in the rainy season. In the dry season, 10.7% of water samples from households and all water samples from ponds, lake and ditches were also contaminated with parasite eggs. The detection of parasite eggs in air was attempted at 156 points (50 points in the house, 88 points outside of the house and 18 points of utility pole). The transparent sticky tape (5x20 cm) was put for two weeks. In the rainy season, parasite eggs were found at 4.9% of the points outside of the house, but parasite eggs were not found in the dry season.

15C-08) STUDY ON THE INTESTINAL PARASITE INFECTION AMONG SCHOOL CHILDREN IN LUANGPRABANG PROVINCE, LAO P.D.R

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In developing countries, the infections of the intestinal parasites (*Ascaris lumbricoides* (As), *Trichuris trichura* (Tt), Hookworms (Hw) and so on) are common diseases and these diseases are very important problems for the health conditions of school children. However in developing countries, the eradication of these parasites is not easy. In this report, we would like to show the best procedure for the treatment of intestinal parasites to the school children in Luangprabang Province, Lao P.D.R. According to the guideline of Lao Ministry of Health, a single dose of mebendazole 500mg is recommended for the treatment method against intestinal parasites. But the stool examination of after treatment is not usually done. Therefore, the effects of mebendazole treatment are not evaluated correctly. In this research, we tried to treat with mebendazole for all children of several schools in Luangprabang Province and evaluated the effect of the mebendazole made in Lao PDR and Thailand. One thousand five hundreds twenty four stool specimens, which were collected from 2,397 school children (11 primary schools) in Luangprabang from September 2003 to May 2005, were examined by Kato's cellophane thick smear technique. On the other hand, the stool examination

was performed for 640 school children at the before and three weeks after treatment with mebendazole. In this treatment, we used three different manufactures of mebendazoles, made in the factory A in Laos (A), the factory B in Laos (B) and the factory in Thailand (T), and we tried two procedures, one was the treatment by a single dose of 500 mg mebendazole (A-500, B-500 and T-500 regime), and another was two-times dosage regime of 250mg once a day for consecutive 2 days (A-250 and B-250 regime).

In the results of before treatments, egg positive rate in 1,524 school children was 93.0% (As 74.5%, Tt 59.6%, Hw 29.8%, *Opisthorchis viverrini* 1.1%, *Taenia* spp. 0.2%), and mixed infection rate was 51.4%. The cure rates of As infection comparing with pre- and post-treatment were over 90% by all methods. On the other hand in Tt infection, B-250 was 30% (T-500, A-500, A-250, B-500 and B-250 were 33.3%, 32.1%, 27.8%, 28.6% and 58.1%, respectively). The cure rates of Hw infection were 40% (T-500), 43% (A-500), 72.2% (A-250), 42.9% (B-500) and 46.4% (B-250). These results suggested that A-250 regime was the most effective against intestinal parasites in these procedures. In the future, we are going to study to obtain the most suitable treatment methods for the intestinal parasites in Lao PDR.

15C-09) STUDY FOR MEBENDAZOLE IN LAO PDR

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Introduction: In our department, therapeutic study of the intestinal parasite infections, such as roundworm, whipworm, hookworm was conducted on the school children of Luangprabang Province in Lao P.D.R., from 2003, and the mebendazole was administered. Based on the therapeutic guideline of intestinal parasite infection of ministry of health, Lao P.D.R., 1 time administration of mebendazole 1 tablet (500mg) was carried out. There may be the dispersion of effect in the difference among the mebendazole of each pharmaceutical company. This time, we examined the quality of the medicine of each pharmaceutical company. We used the mebendazole available in 2 kinds of domestic-product (made in Lao P.D.R.): A and B, 3 kinds of foreign-product: C (made in Vietnam), D (made in Thailand) and E (made in Malaysia). In total, we were able to get 5 kinds of mebendazole tablets in Lao PDR. Actual mebendazole content in the tablet of each pharmaceutical company was measured. Methods: Each tablet was crushed by the mortar, and dissolved in the 0.05% formic acid/ 99.5% isopropanol as 500μg/ml. By analyzing from molar absorption coefficient ε=15000 (312nm; 0.05% formic acid/ 99.5% isopropanol solution), the absorption value of 312nm was measured by the absorbance meter. Each 5 tablets of the pharmaceutical company were measured. Results: It was analyzed from the absorption value, and the content of mebendazole in 1 tablet (500mg) were as follows. A: 563.3±8.0mg, B: 676.7±24.0mg, C: 543.3±11.7mg, D: 356.7±6.3mg, E: 413±8.0mg (Mean±SD). Therefore, it was proven that A, B and C sufficiently contained mebendazole in 1 tablet. The content of mebendazole in D and E were little. On the character of the tablets, C and D were crushable by usual mortar. And, the tablet of B was very easy to smash. A and E were difficult to be crushed (It was physically very firm). Simultaneously, we also got the result of being very characteristic for the property of the tablet of each pharmaceutical company. Discussion: It was important for the mebendazole efficacy to spread easiness to worm directly, since it was not almost absorbed in the gastrointestine. In addition to actual mebendazole content, the character of the tablets, for example, the easiness of the tablet to dissolve may influence the effect of the treatment. We are going to further examine the character of mebendazole tablets of each pharmaceutical company.

15C-10) PARAGONIMIASIS IN LAO PDR.

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Despite of some known cases among refugees outside of Lao PDR, no detail human paragonimiasis research was conducted in these two decades. Yet, no study was performed to identify the species of Paragonimus in the second intermediate host crabs in the country. Therefore, the investigation was performed to clarify this relationship using available crab samples at the central market places and at the northern rural part of Vientiane Capital where paragonimiasis infection had been confirmed. A total of 312 crabs contained 3 genera with 4 species were examined. No metacercaria was recovered from the market obtained 2 Somaniathelpusa spp. (291 and 9 dissected). In the infested area, 100% and 20% of metacercariae infection were confirmed at Potamiscus sp. (7) and Parathelpusa sp. (5), respectivety. In the former crab, 681 metacercariae contained 578 large (L), 99 middle (M) and 4 small (S) size types ones were observed. These metacercariae were mostly distributed in the muscles of there host crabs. The L and M type metacercariae were identified as P. harinasutai and P. bangkokensis, respectively on the basis of their morphological features of metacercariae and adult worms recovered from the experimental dogs. S type and a metacercariae from Parathelpusa sp. were identified as P. heterotremus and P. westermani, respectively on the basis of their morphological features of metacercariae.

Workshop D-3

15D-01) MEASUREMENT OF XANTHURENIC ACID IN ANOPHELINE MOSQUITO

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Xanthurenic acid (XA), a lateral reaction product of tryptophan metabolism in the omochrome pathway of eye pigment synthesis in insects, induces Plasmodium gameogenesis. Previously we reported that XA is present in mosquito salivary glands and that mosquito ingests saliva into the midgut during blood feeding. Taken together, it is likely that XA is discharged with saliva during blood feeding and is swallowed to the midgut where it affects Plasmodium gametocytes. In this study, we used a high performance liquid chromatography with electrochemical detection (HPLC-ECD) to detect and quantify XA. We succeeded to measure XA content in each individual mosquito. One larva or pupa contained 20-50 nanograms (ng) of XA. One female adult contained 10-50 ng of XA. We also measured XA contents in mosquito tissues. The head contained about 70% of XA in the whole body. It is likely because XA is a lateral product of omochrome. The midgut contained 0.1-0.2 ng. The salivary gland contained 0.28 ± 0.05 ng. After blood feeding, XA contents in the salivary gland reduced to 0.13 ± 0.06 ng ($P<0.05$). We suspect that mosquitoes consume saliva with XA on blood feeding and some amount of XA might be swallowed to the midgut.

15D-02) RELATIONSHIP BETWEEN MALARIA TRANSMISSION EFFICACY AND THE AMOUNT OF XANTHURENIC ACID IN ANOPHELINE MOSQUITO

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We succeeded to develop HPLC-ECD method for measuring xanthurenic acid (XA) in mosquito. We can measure XA amount in each individual mosquito. A female adult 7 days after emergence contained 10-14 ng of XA and a male adult contained 4 ng. We collected female mosquitoes when they emerged and measured XA at 2h, 48h, 96h and 240h after emergence. XA contents were highest at 2h after emergence (52 ng) and reduced after that. At 240h XA content was 10 ng. We measured XA in the salivary gland and found 0.35 ng at 48h and 0.10ng at 240h. We let two groups of mosquitoes feed on the same mouse infected with Plasmodium berghei. One group was 2-3 days mosquitoes after emergence (young group), and another group was 10-12 days mosquitoes (old group). Twelve days later, we counted the number of oocysts developed on the midgut. The mean numbers of oocysts were 85 in the youngt group and 25 in the old group. This difference of oocyst number might due to the difference of XA amount swallowed to the midgut.

15D-03) ROBUST EXPRESSION OF A FOREIGN GENE IN THE SALIVARY GLANDS OF ANOPHELINE MOSQUITOES

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Malaria sporozoites invade the mosquito salivary glands and remain in the salivary duct until they are injected with the saliva into vertebrate hosts during blood feeding. The specific mechanisms by which *Plasmodium* parasites

infect the salivary glands remain largely unknown. The purpose of this study was to establish robust salivary gland-specific gene expression in transgenic anopheline mosquitoes and to provide a potential tool for investigating mosquito-parasite interactions. To this end, we obtained a salivary gland-specific promoter from upstream of a gene encoding a saliva protein. A promoter-reporter construct, consisting of the salivary galnd-specific promoter, the *Discosoma sp*. red fluorescent protein (DsRed) reporter gene, and the *Antryp1* polyadenylation signal, was inserted into the *Minos* transfer vector and transformed into the germ line of *Anopheles stephensi* embryos. We generated transgenic *A. stephensi* mosquitoes that specifically express DsRed in their salivary glands. Using advanced 3D confocal microscopy, we showed robust expression of DsRed under control of the salivary gland-specific promoter in the distal-lateral lobes of the salivary glands, where the sporozoites invade preferentially, in a living mosquito as well as in dissected salivary glands. Furthermore, by using GFP-expressing sporozoites, we could observe the parasites passing through the salivary glands from the outer surface. These results open up the possibility of elucidating the process and molecules involved in the salivary gland-parasite interactions, and may lead to the development of transmission-blocking strategies by using genetically modified mosquitoes that express anti-parasitic genes.

15D-04) TRANSGENIC ANOPHELINE MOSQUITOES EXPRESSING LECTIN FORM MARIN ORGANISM IMPAIRE IN TRANSMISSION OF A MALARIA PARASITE

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When a mosquito ingests a blood meal from an infected host, Plasmodium gametocytes transform into gametes that mate and differentiate into zygotes and then ookinetes (elongated motile zygotes). Ookinetes cross the midgut epithelium and differentiate into oocysts, which after 10 -15 days liberate sporozoites cross the salivary gland epithelium. Recent advances in the genetic engineering of anopheline mosquitoes have raised hopes for their use as new strategies for malaria control and provided a powerful tool to investigate mosquito-parasite interactions. Our research on transmission blockade using transgenic mosquitoes has been focused on the midgut stage of the parasites, interfering with ookinete invasion or oocyst differentiation. The molecule that we have introduced into a transgenic mosquito is CEL-III isolated from *Cucumaria echinata* (Marine invertebrate). CEL-III has strong hemolytic activity as well as haemaggrutination activity as a lectin. CEL-III gene expression was driven by the carboxypeptidase promoter, midgut specific promoter. As expected, CEL-III expression was induced in the midgut at 6h after a blood meal. Since CEL-III can hemolyze human and rat red blood cells, but not mouse red blood cells, we established rat-*P. berghei* infection model to address the transmission blocking efficacy of the CEL-III transgenic mosquito. We fed control and transgenic mosquitoes on the same infected rat and measure the numbers of oocysts formed. The transmission blocking efficacy of the transgenic mosquitoes was 91%, as compared with control mosquito. Thus, expression of CEL-III in the mosquito midgut severely reduced vector competency by inhibiting *Plasmodium* development. Because CEL-III targets to red blood cells but not the parasites, we anticipate that this CEL-III transgenic mosquito will be able to impair parasite development of all *Plasmodium* species.

Workshop D-4

15D-05) A REVIEW OF THE SEMINARS FOR TROPICAL MEDICINE AND HYGIENE IN KINKI REGION

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We organized “the seminars for tropical medicine and hygiene in Kinki Region ” once in every 4 to 6 in the last three years. The aims of the seminars are 1. To provide the opportunity for the researchers in Kinki Region to get exposed to various study fields and to promote their communication. 2. To provide the opportunity to learn tropical medicine from the lecturers invited from outside of Kinki Region. 3. To provide practical knowledge of tropical medicine for clinicians and researchers who have experience to work in the field in tropical areas. 4. To help clinicians and related medical staffs who wish to work in the tropical areas in future to contact with researchers working in tropical medicine. With these aims, we have been trying to make the seminars not only as the place of academic discussion but also as an informal place where everyone can attend and speak without hesitation. We held the first seminar in October 2002 with Nishibuchi and Nishiyama as official organizers. The title of the lecture in the seminar was “The present status and preparations for Malaria”. We held seminars eight times so far at the Center for Southeast Asian Studies, Kyoto University and Kansai Medical University in turns usually with two or three lecturers at a time. The followings are the subjects and the numbers (in parenthesis) of the lectures: malaria (3); bacterial infections including Vibrio infection (1), tuberculosis (1), and Hansen disease (1); viral infections including AIDS (1), Arbovirus infection (1), Ebola (1), and SARS (1); mosquito-related diseases (1); field medicine (1), medical care conditions in Laos (4), Bolivia (1), and others (2). We spent enough time to discuss each presentation. Due to limitations in selection of the lecturers there were too many lectures on Laos and no lecture about non-malaria parasitic infections which are very important in tropical area. We should find some ways to solve this problem in the future. The number of the participants was 25.1 on average (range: 18 to 30) per seminar including 9.9 medical doctors, 2.2 nurses and 2.4 medical students. We hope to have more participants from the medical field other than doctors. We are confident that we provided good opportunities for the participants to communicate friendly even after seminar. We will do our best to make this seminar more fruitful.

15D-06) THE TREND OF NEW HIV INFECTIONS AND PATIENTS IN SAKU CENTRAL HOSPITAL

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Preface: The Committee on Trends in AIDS reports that a combined total number of 1165 people newly suffered from HIV infections and AIDS in 2004. By prefecture, Nagano Prefecture ranked second in the number HIV carriers after Tokyo. A tabulation of new reported AIDS patients as against the population rate shows that Nagano came on top of the list. It is expected that the number is great particularly in the eastern part of Nagano Prefecture. The prevalence is looked upon as having been triggered by the influx of foreigners who came en masse for the construction of the Nagano Shinkansen bullet railway line and expressways and for construction projects for the 1998 Nagano Olympic Games. Here, an attempt will be made to show trends in the number of newly infected patients at the Saku Central Hospital, located in the Prefecture’s eastern district, and how the prevalence of HIV stands there.

Results: Our hospital had 74 new HIV carriers from October 1986 to July 2005. They included 47 AIDS patients

(63.5%). The number of patients newly infected with HIV stood at 9 cases in 2004 and 7 cases in January through July in 2005. Of them, those who suffered from AIDS totaled 7 (77.8%) in 2004 and 6 (85.7%) in January through July in 2005. By nationality and gender, the infected had consisted of 8 Japanese men (22.2%), 1 Japanese woman (2.8%), 9 male foreigners (25.0%) and 18 female foreigners (50.0%) before 1999. Since 2000, they have been made up of 26 Japanese men (68.4%), 2 Japanese women (5.3%), 3 male foreigners (7.9%) and 7 female foreigners (18.4%). The infection routes were heterosexuality for 62 patients (83.8%), homosexuality for 2 patients (3.2%), drugs for1patient (1.6%), blood preparations for 1 patient (1.6%), and mother -to-child transmission for 1 patient (1.6%).

Discussion: There have been signs of a rapid rise in the number of new HIV carriers, and things have begun to taken on a serious aspect in which HIV is increasingly carried to Japanese men primarily from foreign women. As relations with opposite sex are responsible in most cases with infections, there is fear for an upswing in the prevalence of HIV infections among Japanese women. Unless convincing measures for the prevention of HIV infections are taken now, they will inevitably sweep the eastern part of Nagano Prefecture in several years.

15D-07) SUMMARY AND PROBLEMS OF TRAINING COURSE FOR DIAGNOSIS OF OPPORTUNISTIC PROTOZOAN INFECTIONS ASSOCIATED WITH AIDS

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We conducted a training course for improvement in the diagnostic techniques and related aspects on opportunistic protozoan infections with the target of medical doctors/ technical personnels in the AIDS network hospitals for these 6 years till 2002 by the financial support from MHLW. This was primarily based on the observation that diagnosis of such infections seemed unsatisfactory due to insufficient education and training as well as rather rare opportunity to encounter these protozoan infections. However, such protozoan infections as amebiasis and toxoplasmosis have been increasingly important in clinical aspects of AIDS. Since 2003, we have expanded the target for training to personnels in general hospitals in addition to the AIDS network hospitals designated by MHLW because of increase in the number of HIV positive cases in our country. For this purpose, we have revised the style and media of announcement of training course and tried to establish the system for self-evaluation and self-motivation by utilizing CD-ROM and the network consultation system. In this presentation, we like to summarize current status of this training course and discuss some essential problems to improve such approaches.

15D-08) SIMULATIONS ON SARS OUTBREAK IN JAPAN USING THE MATHEMATICAL MODEL

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We had a worldwide outbreak of the severe acute respiratory syndrome (SARS) raised from Hong Kong in March, 2003. In Japan, 52 susceptible cases as well as 16 possible cases of SARS-infected patients had been reported from hospitals although no Japanese had consequently been decided as SRAS-infected patients. However, we Japanese can never negate the possibility that SARS will invade and sweep over Japan. It is therefore important to investigate the spread of SARS under an epidemic in Japan in an attempt to devise effective measures against SARS. The two re-

markable risk factors of SARS-transmission are well-known; one is super-spreader events (SSE), another is so-called “close contact”, especially in hospitals. In this study, we applied mathematical stochastic models based on these risk factors for the simulation of the events of SARS transmission in Tokyo 23 wards of Japan. In the SSE invasion model, the initial patient expands SARS to 15 people within only one day. In the nosocomial transmission model, the transmission is influenced by the period until when SARS-infected patients are sequestered. One SARS-infected patient transmits SARS to 20 persons under no sequestration. The daily numbers of new incidents and prevarent cases were simulated in each model. The periods from infection to onset, from onset to admission, from admission to discharge and from admission to death referred to the previous case reports and were fitted by Gamma distributions. Our SSE invasion model shows that the maximum expected daily numbers of new incidents and prevarent cases are 51 and 782 people, respectively, for the case of a SSE invasion, while they are 8 and 126 people for a non-SSE. In nosocomial model, they are 4 and 27 people for the case of 6 days of non-isolation of SARS-infected patients and 19 and 121 people for 12 days of non-isolated situation respectively. In Tokyo 23 wards there are 64 beds in negative pressure rooms available. Our models indicate that patients fill them entirely on the 17th day in the case of 12 days -non-isolation of nosocomial model, as well as on the 20th day for the case of a SSE invasion and on the 35th day in case of a non-SSE invasion in SSE invasion model. It is important for prevention of expansion of SARS infection both to find out SARS infection at immediate early days and devise measures against the transmission of SARS as soon as possible.

15D-09) TRAVEL MEDICINE OF GENERAL PRACTICE IN JAPAN

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Not received

15D-10) HOW WELL TRAVEL CLINICS ARE KNOWN AMONG TRAVEL AGENCIES

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As internationalization increases, and overseas travel becomes more affordable, the number of Japanese travelers is growing. Despite the risk of contracting new diseases, or aggravating chronic disorders, Japanese travelers show little concern about health matters. The purpose of this survey was to ascertain how well travel clinics are known among Japanese travel agencies.

[Methods]

We conducted a survey by sending a questionnaire to 660 travel agencies belonging to the Japan Association of Travel Agents (JATA) in March 2005. The following information was requested in the questionnaire.

1. Characteristics of travel agencies
2. How well travel clinics are known among travel agencies
3. How necessary travel agencies think travel clinics are.
4. Services travel agencies expect from travel clinics.

[Results]

60 travel agencies agreed to participate in this survey (participation rate of 9%).

(1) Characteristics of travel agencies: The average number of clients per month was 4390. Main destination of their tours was Asia (68.3%), Europe (8.3%), North America (6.7%), Oceania (3.3%). The duration of the stay was less

than 7 days for many travel agencies (81.6%). Half of Travel agencies had any organized tours for travelers with health problems. (aged 33.3%, disabled 18.3%, hemodialysis 8.3%, home oxygen therapy 3.3%)

(2) More than half of the travel agencies were uinaware of the existence of travel clinics.

(3) Approximately a quarter of travel agencies said they would like to utilize travel clinics.

(4) The majority of travel agencies expected travel clinics to provide them with medical information for travelers before they departed and wanted to be able to consult clinics about health problems their clients experienced while traveling.

A small percentage of travel agencies expected clinics to administer vaccinations to travelers.

[Conclution]

The majority of them are unaware that travel clinics exist and as a result, they expect very little from the clinics at present. In the future, JOHAC would like to circulate information about travel clinics to promote their use. Japan needs to be equipped with a system for dealing with travelers'health issues

15D-11) CHEMOPROPHYLAXIS ACCORDING TO THE GUIDELINES ON MALARIA PREVENTION FOR JAPANESE OVERSEAS TRAVELERS

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Mefloquine (Mephaquine Esu-Esu / Hisamitsu 275) has been approved and registered as a chemoprophylaxis against malaria since 2001 in Japan, and in March 2005, the guidelines on the prevention of malaria for Japanese overseas travelers was finally published by the group of specialists on malaria under the auspices of Japanese Society of Tropical Medicine and Ministry of Health, Labour and Welfare of Japan. Now, we have implemented the pre-travel consultation on malaria as a part of travel clinic services in the International Medical Center of Japan (IMCJ) since October 2004. We reported in this meeting the current situation of chemoprophylaxis against malaria according to the guidelines on the clients who came to our clinic. Through October 2004 to June 2005, 52 clients came to see us in our clinic prior to their departure of travel abroad, asking chemoprophylaxis. According to the Guidelines, Mefloquine was administered to 27 clients, of which 22 were definitely thought to need regular chemoprophylaxis. Mefloquine was not advised to the rest of the 25 clients, because the durations of their stays were too long to avoid possible side effects, or to the contrary, too short to be symptomatic during their travel. Indeed, some of the destinations were free from malaria. Out of the 27 Mefloquine administered clients, 7 (26%) showed side effects such as headache, vertigo and nausea, but 17 (63%) did not. Great diversity of malaria risks regarding the various travel plans of Japanese travelers makes it very difficult to administer appropriate chemoprophylaxis to the clients. The Guidelines were proved to be useful for the advice, but further practice and experiences in malaria chemoprophylaxis were still needed for the doctors to perform more reliable pre-travel consultation.