

## US-Japan Cooperative Medical Science Program and Research on Tropical Disease

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### **1. Organization of the USJCMSP**

US-Japan Cooperative Medical Science Program (USJCMSP) was initiated in 1965 under the agreement between the summit of two countries, then Prime Minister of Japan Mr. E. Satoh and then president of the US Mr. L. Johnson. The aim of the program was to initiate cooperative research between the two countries on diseases prevalent in Asia. Joint delegation committee was organized in both countries consisting of biomedical experts and administrators, and five joint research panels were formed under the program, namely, cholera, leprosy, parasitic diseases, tuberculosis and viral diseases. The joint committee met once a year either in the US or in Japan, and the Sub-committee on Program Review and Planning met twice, once immediately before the joint committee meeting and another one intermediately in Hawaii, usually in January or February.

Each panel consists of five panel members including its chair from both sides and some 25 collaborative researchers in case of Japan, and research activities of each panel are carried out according to the guideline set for each panel by the joint committee. The guideline could be revised according to the recommendation of the joint committee. Each panel held the joint research conference annually and alternately in Japan and in the US. The budget of the USJCMSP of the Japanese side includes research grant, travel expense for the joint research conference, dispatch of scientists to the US and Asia.

### **2. Development of the USJCMSP**

In 1966, the malnutrition panel was newly added considering the serious nutritional situation in Asian countries. In 1970, five years after the initiation of the program, it was decided to carry out review on panel research activities, and in 1971, the guideline for the review was approved, and actual review was initiated on leprosy and parasitic diseases panels. In 1971, it was also recommended to establish a new panel on environmental mutagenesis and carcinogenesis panel taking into account the deterioration of environmental situation in Asian countries in accordance with the economic development, in particular the progress of industrialization, and in 1972, it was agreed to create a new panel on environmental mutagenesis and carcinogenesis.

In 1977, the name of the cholera panel was changed to the cholera and related diarrheal diseases panel as the results of the review of panel activities because research had been expanded to toxins of *E. coli* causing diarrhea similar to cholera.

It was also suggested to create a new independent panel on hepatitis as it was a serious problem in most Asian countries though it was caused by viruses. In 1978, a joint symposium on hepatitis was held in conjunction with the joint committee, and after hearing presentations in the symposium, it was recommended to create a new panel on hepatitis. The Japanese translation of the malnutrition panel was changed from "low nutritional status" to "abnormal nutritional status", as the research activities of the panel started to cover such problems as obesity. In 1979, a new panel on hepatitis was established.

In 1980, a symposium on immunology was held in conjunction with the joint committee meeting, as there had been a marked progress in the research on immunology, and such a progress had been applied in the research activities of each panel. In 1981, the new immunology board was established. Administratively, the delegation committee is under the jurisdiction of the Ministry of Foreign Affairs, the panels are under the Ministry of Health and Welfare, and the new immunology board is under the Ministry of Education, Culture and Sports, and the budget is provided separately by these ministries.

In 1988, the new panel on AIDS was established considering the serious situation of HIV/AIDS. In 1993, a workshop on acute respiratory infection was held, as ARI and diarrhea were two top killers in most developing countries and the former was not yet included in the USJCMSP. A workshop on ARI was held again in 1994, and a workshop on measles was held in 1995. Hearing presentations and discussions in these workshops, it was felt necessary to create a new panel on ARI, however, it was difficult to increase the number of panels under the financial situation of Japan. In 1996, the TB and leprosy panels were amalgamated into one TB and leprosy panel and a new panel on ARI was established. During the transition period for five years, the TB and leprosy panel had two co-chairs on each side and the number of panel members and collaborative researchers is larger than the ordinary panel, however, it will be reduced to normal size within five years.

In 1997, the name of malnutrition panel was changed to the nutrition and metabolism panel as diabetes mellitus became one of serious problems in developing countries and it should be included in the activities of the panel.

In July 1998, a workshop on immunity and infection was held in conjunction with the joint committee meeting, and interesting overview was made on the topic. The name of the cholera and related diarrheal diseases was changed to the cholera and other enteric bacterial infection panel as viral diarrhea is studied in the viral diseases panel.

### **3. Emerging and re-emerging infectious diseases and the USJCMSP**

In April 1996, during the summit talk of the Prime Minister of Japan Mr R Hashimoto and the president of the US Mr B Clinton, it was agreed to include a topic of emerging infectious diseases into the common agenda between two countries, and the USJCMSP was mandated to cope with this topic from scientific aspect.

In July 1996, the first international conference on emerging infectious diseases in the Pacific rim was held in Kyoto soon after the joint committee meeting held in Hiroshima under the sponsorship of the USJCMSP, and the overview was made on major emerging and

re-emerging infectious diseases. As big epidemic of EHEC O-157 was ongoing in Japan during this time, the mass media of Japan showed keen interest on this topic.

In March 1997, the second international conference on emerging infectious diseases in the Pacific rim was held in Bangkok under the sponsorship of the USJCMSP, and topics discussed during this conference were dengue and dengue haemorrhagic fever, infection with EHEC O-157 and resistance to antimicrobials. It was possible to invite some research workers from Asian countries to this conference.

In March 1998, the third international conference on emerging infectious diseases in the Pacific rim was held in Denpasar, Bali. Topics discussed were malaria, TB, hepatitis and the relationship between the infection and malignancy. It was possible to invite much more participants from Asian countries than the last year.

How major emerging and re-emerging infectious diseases are dealt in the panels of the USJCMSP could be summarized as follows:

Cholera and other enteric bacterial infection panel: Active joint research activities are made on the infection with EHEC O-157 and a new strain of vibrio cholerae O-139.

TB and leprosy panel: TB is a typical re-emerging infection, and active research is carried out on the development of rapid diagnostic methods and molecular level mechanism of tuberculoimmunity.

Viral diseases panel: Ebola haemorrhagic fever is one of typical emerging infections, however, it is rather difficult to study it in Japan. Dengue and dengue haemorrhagic fever is a typical re-emerging infection, and active research is ongoing under the USJCMSP.

Parasitic diseases panel: Malaria is also one of important re-emerging diseases, and the emphasis of research is focussed on the development of a new vaccine.

Environmental mutagenesis and carcinogenesis panel: *Helicobacter pylori* infection is one of emerging infections, and its relation with not only the emergence of gastric ulcer but also on gastric cancer is a hot area for research.

Hepatitis panel: Hepatitis viruses E and C are newly identified, and studies on these new viruses are ongoing.

AIDS panel: HIV/AIDS is one of typical emerging infections, and active researches are ongoing including the development of new vaccines and drugs. HTLV-1 is also a new virus isolated in Japan, and it is investigated in this panel.

#### **4. Role played by the USJCMSP for researches in tropical diseases**

During 1960s and 1970s, interest on tropical diseases were reduced in Japan due to the rapid decrease of the diseases, and many departments of parasitology or infectious diseases were closed in the medical school. Under such circumstances, the USJCMSP contributed to maintain research capability for tropical diseases. If there were no USJCMSP, much more departments on parasitology or infectious diseases might disappear from the medical school.

Each panel held joint research conference with the US panel every year, and this was a good occasion to expose young Japanese scientists to the international world and encourage them to participate more actively in the research on tropical diseases.

Real collaboration in research has been made between scientists of two countries by exchanging bacterial strains, antigens and other materials, and conducting complementary researches.

Through the communication program under the USJCMSP, Japanese scientists had a chance to visit the US or Asian countries to observe and discuss about the ongoing researches on tropical diseases. It is our regret that the communication and exchanges of scientists are one-sided, mostly from Japan to the US, and it is our wish to invite more US scientists to work with us in Japan.

Although our target are diseases prevalent in Asia, it was rather difficult to involve Asian scientists to the USJCMSP mainly due to insufficient research grant, however, in a recent few years after the introduction of the emerging infectious diseases to the USJCMSP, it has become possible to invite several Asian scientists and health administrators to the symposium, and we are now considering to initiate the collaborative research on emerging and re-emerging infectious diseases with Asian scientists.

## **5. Major achievements of the USJCMSP on tropical diseases**

Cholera and other enteric bacterial infection panel: Development of oral rehydration therapy, characterization of cholera toxin and its application to the development of vaccine, and studies on EHEC O-157 and vibrio cholerae O-139.

Hepatitis panel: Identification of hepatitis viruses C and E, the production of vaccine against hepatitis B, and studies on the treatment of chronic hepatitis B, C and D by alpha interferon.

Tuberculosis and leprosy panel: Elucidation of cellular and molecular mechanism of tuberculoimmunity, new methodologies in molecular epidemiology such as RFLP, development of animal models for leprosy and multi-drug therapy.

AIDS panel: Development of *in situ* PCR and other single cell techniques which enabled to detect a large number of CD4+ lymphocytes and monocyte/macrophages infected with HIV virus. Advances in the development of chemotherapy and vaccines for HIV infection.

Environmental mutagenesis and carcinogenesis panel: Development and application of new animal models and short-term tests to screen new mutagens and carcinogens and their identification, monitoring mutagens and carcinogens in human population, and studies on interaction between cancer and infections.

Viral diseases panel: Development of a new vaccine against rabies, field trial of preventing dengue and dengue haemorrhagic fever, and studies on viral gastroenteritis.

Parasitology panel: Demonstration of the role of cytokines in protective immunity and disease progression during parasitic infections, and identification of defined recombinant and/or synthetic antigens that induce protective immunity against malaria, schistosomiasis and filariasis.

## **6. Future direction of the USJCMSP relating to research in tropical diseases.**

Since 1998, a new budget was mandated to the Japanese delegation of the USJCMSP

through the Ministry of Health and Welfare in addition to the regular budget. This budget is called the supporting budget for the internationally priority strategic research, and its aim is to support priority research under the USJCMSP, thus to promote health of Asian people.

The budget could be used for the following activities:

- 1) To sponsor international conference on emerging and re-emerging infectious diseases,
- 2) To prepare for the above conference,
- 3) To support researches on priority topics, and
- 4) To dispatch Japanese experts overseas or to invite foreign researchers if urgently needed.

Through this budget, it has become possible for each panel to use approximately 1 million Yen for each year for collaborative research with Asian scientists on priority topics. Though the amount of research grant is very small, if we could show excellent achievements in this collaborative research, it might be possible further to increase the budget in the future.