ISSN 0304-2146

日本熱帯医学会雑誌

Japanese Journal of Tropical Medicine and Hygiene

第14巻 第2号　　昭和61年6月15日

内　　容

日熱医会誌
Japan. J. T. M. H.

日本熱帯医学会

Japan. J. Trop. Med. Hyg., Vol. 14, No. 2, 1986, pp. 79–86

TWO UNKNOWN MARINE SPECIES OF THE GENUS *DIPHYLLOBOTHRIUM* FROM HUMAN CASES

HAJIME KAMO[1], SEIICHI YAZAKI[1], SOJI FUKUMOTO[1], JOJI MAEJIMA[1] AND YUJI SAKAGUCHI[2]

Received March 22 1986/Accepted May 15 1986

Abstract: The morphological characteristics of two unknown marine species of the genus *Diphyllobothrium* were recorded. A cestode spontaneously expelled from a 27-year-old seaman resembled *D. cameroni* Rausch, 1969 from a Japanese seaman by Kamo *et al.* (1981) in the external morphology, but was different in the relative position of the uterine pore. It was related to *D. hians* (Diesing, 1850) in the position and shape of the cirrus sac, and in the relative position of the cirrus sac to the seminal vesicle, but was different in the shape and size of the scolex. Another cestode expelled after treatment with kamala from a 50-year-old seaman resembled *D. hians* in the shape of proglottids, the development of inner longitudinal muscle layer, the position of genital atrium, the uterine loops, and egg-sizes. This was rather related to *D. elegans* (Krabbe, 1865) in the shape and position of the cirrus sac and the relative position of the cirrus sac to the seminal vesicle, and was different from *D. hians* in these characteristics. The definite identification should be established in the future on the basis of more detailed materials and methods.

INTRODUCTION

Sakaguchi *et al.* (1971) have reported five human cases infected with diphyllobothriid cestodes found from the inhabitants of fishing villages in Nagasaki Prefecture, Japan. Three of those cestodes had been identified as *Diplogonopurus grandis,* while the remaining two had been taxonomically indeterminable. Later Kamo *et al.* (1979) observed the densely distributed deep pits of their eggshell surfaces by the use of scanning electron microscope, suggesting their association with marine environments.

Since Kamo *et al.* (1977) suggested the occurrence of human infection with a certain species of *Diphyllobothrium* of marine origin, a few marine species of the genus *Diphyllobothrium* have been recorded from human cases in Japan such as *D. yonagoense* by Yamane *et al.* (1981), *D. cameroni* by Kamo *et al.* (1981), and *D. pacificum* by Kamo *et al.* (1982). The morphological characteristics of both specimens under consideration were different from those known species of marine origin in Japan. Moreover, they were not identical with descriptions of any other known species from marine mammals.

Then their morphological characteristics were recorded here for further comparison and identification.

1 Department of Medical Zoology, Tottori University School of Medicine, Yonago 683, Japan
2 Department of Parasitic Diseases, Kumamoto University Medical School, Kumamoto 860, Japan

Materials and Methods

Case No. 1: On 10th October, 1969 a strobila with the scolex has been expelled spontaneously from K. Y., a 27-year-old seaman, who resided at Kami-Goto-Machi, Nagasaki Prefecture. The yellowish-brown stout worm measured 460 mm in length, 12.5 mm in maximum width, and 1.8–2.0 mm thick.

Case No. 2: On 26th November, 1969 a cestode without the scolex has been expelled after treatment with kamala from I. Y., a 50-year-old seaman, who resided at Ko-Yagi-Machi, Nagasaki Prefecture. The milkish-white, thin worm was undulated, measuring 1,020 mm in length and 7.0 mm in maximum width.

The worms have been preserved in formalin solution. Whole mount preparations of various maturity-levels of proglottids were stained with Semichon's acetic carmine. Serial sections of mature proglottids were prepared in horizontal, sagittal and transversal planes, being stained with modified trichrome stain solution. The eggshell surfaces were observed by the scanning electron microscopy.

Morphological Descriptions

(All measurments given are in millimeters)

Cestode from Case No. 1: Contracted specimen with scolex, body length 460, lacking terminal segments, maximum width 12.5, maximum thickness about 2.0 (Figure 1).

Strobila muscular, slightly arched dorsad; margins slightly serrate. Strobila composed of as many as 500 segments; maximum width attained near terminal one fourth of strobila. Segments

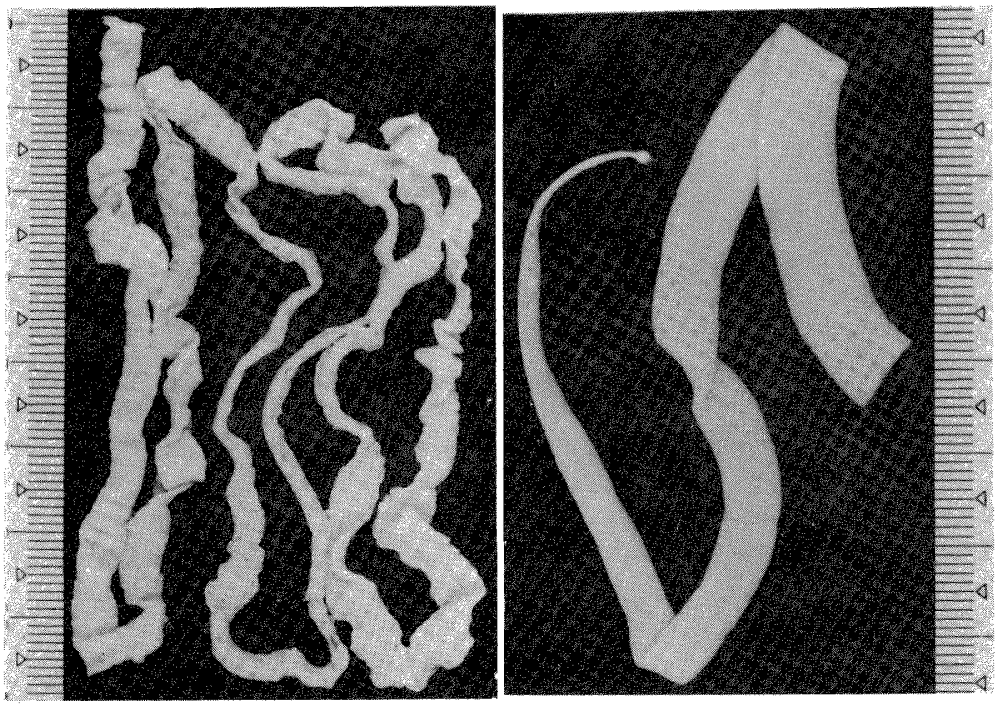

Figure 1 Whole body: specimen No. 1 (left), No. 2 (right).

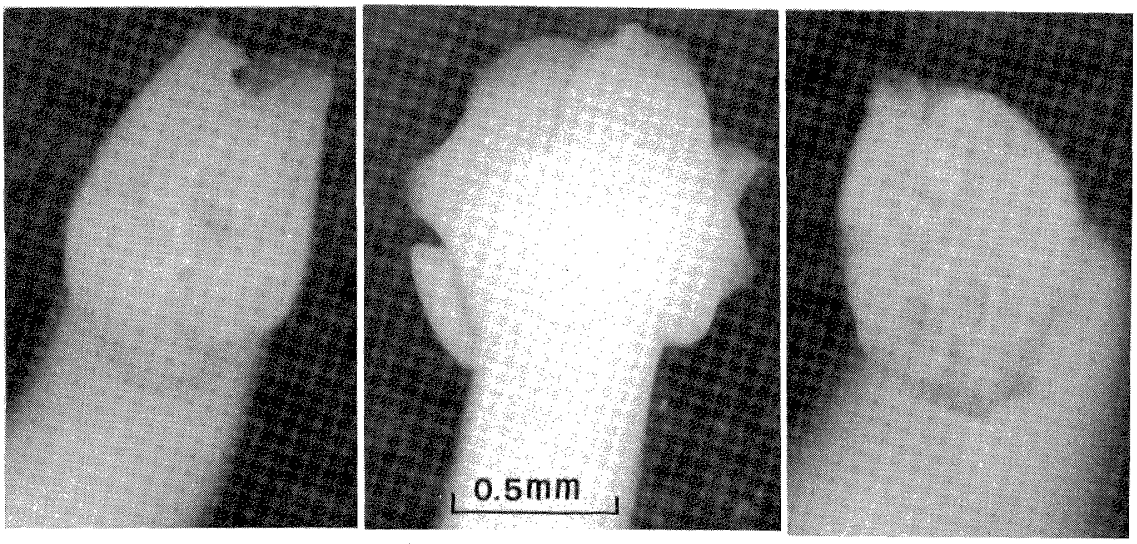

Figure 2 Scolex of specimen No. 1: dorsoventral view (left), lateral view (middle), and apical view (right).

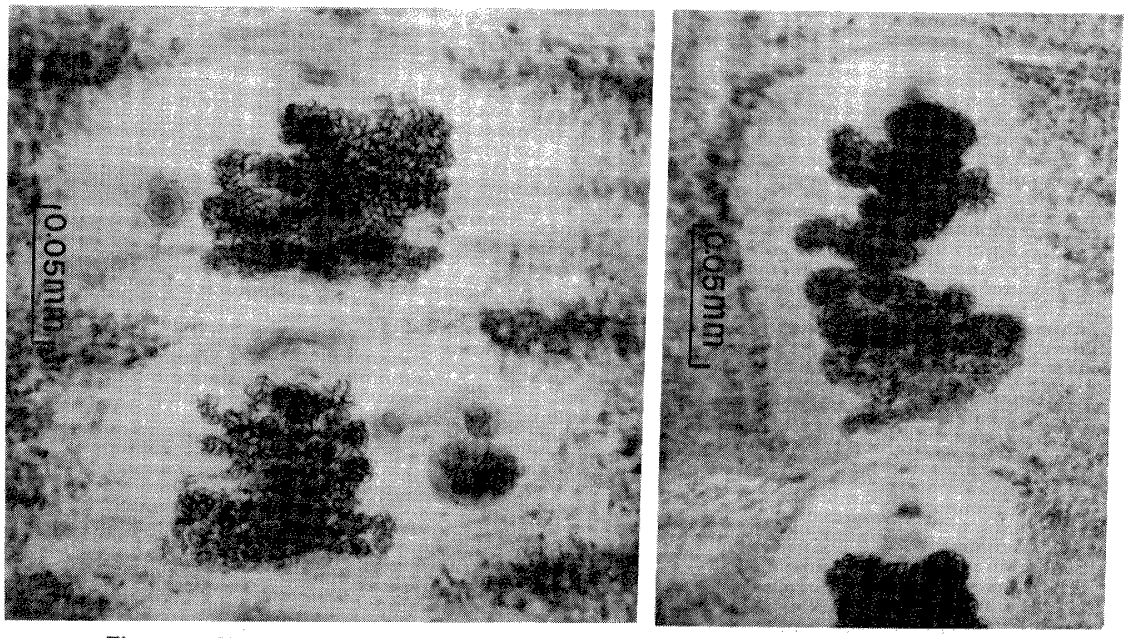

Figure 3 Uterine field of mature segment: specimen No. 1 (left), and No. 2 (right).

wider than long, with length increasing posteriad. Length/width ratio of pregravid segments about 1 : 15; of terminal gravid segments about 1 : 10. Innermost layer of longitudinal muscle fibres well developed, as much as 0.288 thick; adjacent layer of circular fibres fairly developed (Figure 4). Calcareous corpuscle abundant. Polygonal scolex, with deep bothria extending full length, 1.08 long×1.13 wide in lateral view. Bothria with folded margins diversing at apex (Figure 2). Neck absent; posterior edge of scolex slightly overlapping first segment. Genital pore visible within 70 mm posterior to scolex, situated ventrally on midline at anterior margin of segment, covered by velum of preceeding segment (Figure 3). Genital atrium lined by rounded papillae. Cirrus sac elongate, with margins somewhat undulating in sagittal sections, 1.123–

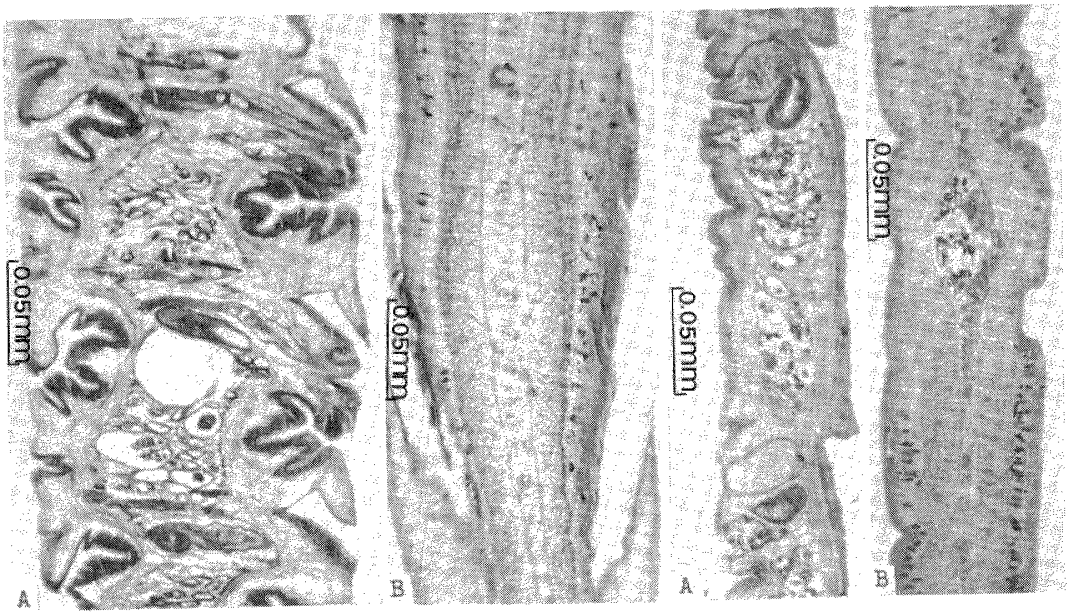

Figure 4 Sagittal (A) and cross (B) sections: specimen No, 1 (left) and No. 2 (right).

1.164 long×0.098–0.133 in diameter. Seminal vesicle elongate, 0.412–0.525 in dorsoventral dimension by 0.124–0.139 in diameter, situated adjacent and parallel to cirrus sac posteriorly, and connected with latter by short duct (Figure 4). Subspherical testes numerous, 0.103–0.175 in greatest diameter, arranged in single layer in lateral fields. Terminal portion of vagina running anteriad, then turning ventrad into genital atrium and opening posterior to opening of cirrus sac. Bilobed ovary situated transversely near posterior margin of segment. Vitelline follicles (vitellaria) abundant, forming two lateral fields, 0.052–0.072 in greatest diameter. Gravid uterus forming compact loops extending through length of segment from posterior margin to level of anterior edge of genital atrium (Figure 3). Uterus opening through uterine pore posterior to genital pore, usually to right or left of midline. Eggs ellipsoidal to subspherical with apical knob, 0.046–0.056×0.033–0.044 (avg. 0.049±0.02×0.036±0.03). Surface of egg-shell densely distributed by broad pits (Figure 5).

Cestode from Case No. 2: Slightly contracted specimen without scolex, body length 1,020, maximum width 7.0 (Figure 1).

Strobila somewhat muscular, with slightly serrate margins. Segments wider than long, with slightly convex margins, increasing relative length near posterior end of strobila. Length/width ratio of mature segments about 1 : 5, of gravid segments 1 : 3.5, and of terminal gravid segments 1 : 1.5. Innermost layer of longitudinal muscle fibres well developed, about 0.185 thick; adjacent layer of circular fibres fairly developed (Figure 4). Calcareous corpuscle abundant. Genital pore situated ventrally on midline in near anterior margin of segment (Figure 3). Genital atrium lined by rounded papillae. Cirrus sac piriform, with margins somewhat undulating wall, 0.484–0.567 long×0.288–0.391 in diameter. Cirrus sac opening anteriorly into genital atrium. Seminal vesicle subspherical, situated posterior to end of cirrus sac, 0.309–0,433 long ×0.175 in diameter (Figure 4). Subspherical testes numerous, 0.082–0.103 in greatest diameter, arranged in single layer in lateral fields. Terminal portion of vagina running anteriad near ventral surface, turning slightly ventrad into genital atrium immediately posterior to opening of

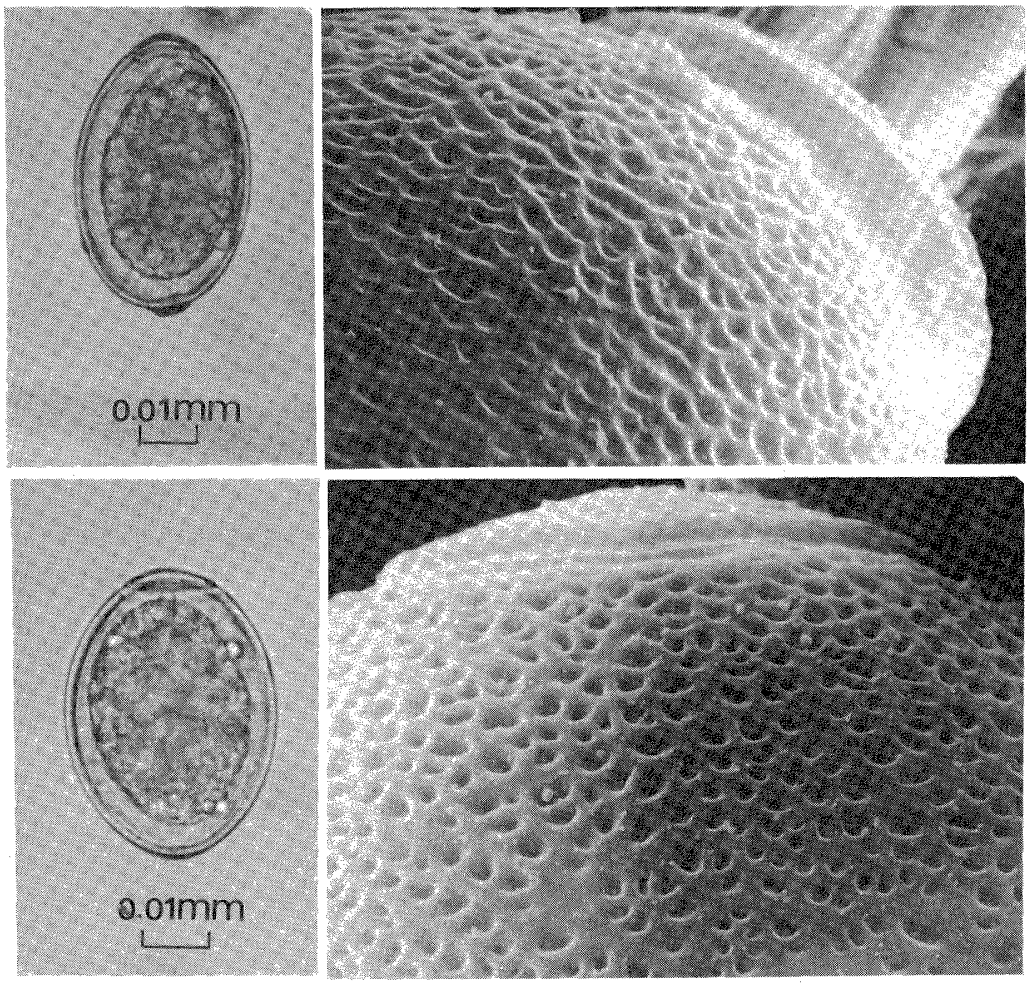

Figure 5 Eggs and eggshell surfaces by SEM (×5,000): specimen No. 1 (upper), and No. 2 (lower).

cirrus sac. Bilobed ovary situated transversely near posterior margin of segment. Vitelline follicles abundant, forming two lateral fields, 0.052–0.072 in greatest diameter. Gravid uterus forming compact loops extending through length of segment from posterior margin to level of anterior edge of genital atrium (Figure 3). Uterus opening through uterine pore posterior to genital pore usually to right or left of midline. Eggs subspherical with or without apical knob, 0.043–0.048×0.033–0.039 (avg. $0.044 \pm 0.02 \times 0.035 \pm 0.02$). Surface of eggshell densely distributed by broad pits (Figure 5).

Discussion

Judging from the nature of their eggshell surfaces our specimens can be recognized as members of the genus *Diphyllobothrium* associated with marine environments (Hilliard, 1972).

In regard to the marine species of *Diphyllobothrium* from human cases the following 6 species have been reported so far: *D. cordatum* (Leuckart, 1863) from Greenland by Leuckart (1863); *D. alascense* Rausch et Williamson, 1958 and *D. lanceolatum* (Krabbe, 1865) from Alaska by Rausch and Hilliard (1970); *D. pacificum* (Nybelin, 1931) from Peru by Baer *et al.* (1967),

from Chile by Atias and Cattan (1976), Sagua *et al.* (1976), from Japan by Kamo *et al.* (1982); *D. yonagoense* Yamane *et al.*, 1981 and *D. cameroni* Rausch, 1969 from Japan by Yamane *et al.* (1981) and Kamo *et al.* (1981), respectively.

Of these *D. cameroni* Rausch, 1969, especially the specimen found from a Japanese seaman (Kamo *et al.*, 1981) resembles our specimen from the Case No. 1 in the external morphology. In histological details, however, the relative position of the uterine pore, *D. cameroni* is different from our specimen No. 1. The uterus opens into the genital atrium in *D. cameromi,* while it opens separate from and posterior to the genital atrium in our specimen No. 1.

According to the recent revision of diphyllobothriid cestodes by Delamure *et al.* (1985) 29 species of the genus *Diphyllobothrium* were recognized as valid, though a few of them are debatable.

Including the above-mentioned human parasites 23 species of them can be comprised in a group of marine origin. Most of them have special characteristics respectively in their external and/or internal morphology, and are distinguishable enough from our specimens. *D. hians* (Diesing, 1850) among them resembles our specimen No. 1 in the position and shape of the cirrus sac, and the relative position between the cirrus sac and the seminal vesicle, but is apparently different in the shape and size of the scolex.

D. hians is also related to our specimen from the Case No. 2 in the shape of proglottids (length/width ratio), the development of inner longitudinal muscle layer, the position of genital atrium, the uterine loops, and egg-sizes. However, the shape and position of the cirrus sac, and the relative position between the cirrus sac and the seminal vesicle resemble more other species: *D. elegans* (Krabbe, 1865).

Thus our specimens are both seemed to be distinctive from all known species, but the definite identification should be established in the future on the basis of more detailed materials and methods.

Acknowledgements

The authors wish to express our heartfelt thanks to Prof. emeritous D. Katamine and Prof. Y. Aoki, Department of Parasitology, Institure of Tropical Medicine, Nagasaki University, for their kindness and encouragements through providing with specimens. To Mrs. S. Wakahara, Mr. Y. Sugihara, and Miss Y. Yakura, Department of Medical Zoology, Tottori University School of Medicine, appreciation is expressed for their technical assistances.

References

1) Atias, A. and Cattan, P. E. (1976): First case of human infection with *Diphyllobothrium pacificum* in Chile, Rev. Méd. Chile, 104, 216–217
2) Baer, J. G., Miranda, C. H., Fernández, R. W. and Medina, T. J. (1976): Human diphyllobothriasis in Peru, Z. Parasitenkd., 28, 277–289
3) Delamure, S. L., Skriabin, A. S. and Serdyukov, A. M. (1985): Diphyllobothriid cestodes from humans, mammals and birds, 51–137, Nauka, Moscow (in Russian)
4) Hilliard, D. K. (1972): Studies on the helminth fauna of Alaska LI. Observations on eggshell formation in some diphyllobothriid cestodes, Can. J. Zool., 50, 585–592
5) Kamo, H., Maejima, J., Yazaki, S., Fukumoto, S. and Hiraga, M. (1979): Another marine species of *Diphyllobothrium* found from 3 seamen in Kyushu, Jap. J. Parasit., 28, supp., 74 (in Japanese)

6) Kamo, H., Maejima, J., Yazaki, S., Otsuru, M., Hasegawa, H., Kuniyoshi, Sh. and Asato, R. (1982): Occurrence of human infection with *Diphyllobothrium pacificum* (Nybelin, 1931) Margolis, 1956 in Japan, Jap. J. Parasit., 31, 165–170 (in Japanese)
7) Kamo, H., Yamane, Y. and Kawashima, K. (1981): The first record of human infection with *Diphyllobothrium cameroni* Rausch, 1969, Japan. J. Trop. Med. Hyg., 9, 199–205
8) Kamo, H., Yamane, Y., Maejima, J., Yazaki, S. and Fukumoto, S. (1977): "Koga-Okamura type" diphyllobothriid cestode other than *D. latum* found from human cases in Japan, Nippon-Iji-Shimpo, 2795, 43–45 (in Japanese)
9) Leuckart, R. (1863): Die menschlichen Parasiten und die von ihnen herrührenden Krankheiten. Ein Hand und Lehrbuch für Naturforscher und Aerzte, Vol. 1, 766, C. F. Winter's Verlag, Leipzig und Heidelberg
10) Rausch, R. L. and Hilliard, D. K. (1970): Studies on the helminth fauna of Alaska XLIX. The occurrence of *Diphyllobothrium latum* (Linnaeus, 1758) (Cestoda: Diphyllobothriidae) in Alaska, with notes on other species, Can. J. Zool., 48, 1201–1219
11) Sagua, H., Miranda, E., Fuentes, A. and Vladillo, V. (1976): *Diphyllobothrium pacificum* (Nybelin, 1931) Margolis, 1956. First two human cases of infection in Northern Chile, Bol. Chile. Parasit., 31, 33
12) Sakaguchi, Y., Harada, T. and Muta, N. (1971): A description of tapeworms (Diphyllobothriidae) occuring in Nagasaki Prefecture, Jap. J. Parasit., 20 (1), supp., 31–32 (in Japanese)
13) Yamane, Y., Kamo, H., Yazaki, S., Fukumoto, S. and Maejima, J. (1981): On a new marine species of the genus *Diphyllobothrium* (Cestoda: Pseudophyllidea) found from a man in Japan, Jap. J. Parasit., 30, 101–111

人寄生海洋性裂頭条虫の未知種2例

加茂　甫[1]・矢崎　誠一[1]・福本　宗嗣[1]
前嶋　條士[1]・坂口　祐二[2]

人寄生海洋性裂頭条虫の未知種2例について，それらの形態的特徴を記録した。27歳男子船員から自然排出された条虫は，外形が日本人船員から前に見出された *D. cameroni* と近似しているが，子宮孔の相対的位置が異なる。その陰茎嚢の位置や形，陰茎嚢と貯精嚢の相対的位置は *D. hians* と似ているが，頭節の形や大きさが異なる。50歳男子船員からカマラにより駆出された条虫は，片節の縦横比，内側縦走筋層の発達度，生殖孔の位置，子宮ループ，虫卵の大きさなどが *D. hians* と似ているが，陰茎嚢の位置や形，陰茎嚢と貯精嚢の相対的位置は異なり，これらの点はむしろ *D. elegans* と似ている。確定的な同定は将来を期したい。

1 鳥取大学医学部医動物学教室　　2 熊本大学医学部寄生虫病学教室

Japan. J. Trop. Med. Hyg., Vol. 14, No. 2, 1986, pp. 87–90

BENIGN TERTIAN TYPE MALARIAS (*P. OVALE* AND *P. VIVAX*) CONTRACTED IN AFRICA

ISAO EBISAWA

Received March 7 1986/Accepted May 10 1986

Abstract: Twenty-one cases of ovale malaria were seen among 25 patients of benign tertian malaria contracted during visits to African countries, south of the Sahara. This reflects an increase in the number of Japanese visiting this area as *P. ovale* is, with a few exceptions, endemic only in tropical African countries. Nigeria, Malawi and Guinea were the most frequent countries of infection with 6, 4 and 3 cases, respectively.

One patient each with vivax malaria was infected in Malawi, Guinea and Mali; one case was infected in the island country of Madagascar in East Africa.

Because both *P. ovale* and *P. vivax* exist in tropical African countries, we stress the importance of careful examination of blood smears when diagnosing malaria.

INTRODUCTION

The benign tertian malaria parasite most prevalent in tropical Africa is *P. ovale,* which is, with a few exceptions (Jeffery *et al.*, 1954; Wilcox *et al.*, 1954; Jeffery and Young, 1954; Lysenko and Beljaev, 1969) endemic only on this continent (Report of a WHO Scientific Group, 1969; Garnham, 1966).

Japanese patients infected with *P. ovale* began to appear in 1971 (Amano *et al.*, 1972; Ebisawa *et al.*, 1972, 1973). The total number of ovale malaria patients seen by the author rose to 21 by the end of 1985, reflecting an increase in the number of Japanese visiting this area.

However, during a review of my case records of malaria patients, 4 cases having been infected with *P. vivax* contracted in tropical Africa came to my attention; obviously both *P. ovale* and *P. vivax* were prevalent in the same tropical African countries.

The purpose of this paper is to report the areas where my patients were infected with *P. ovale* and also to call attention to the fact that both *P. ovale* and *P. vivax,* which is rarely pathogenic to the black people (Jeffery and Young, 1954), are circulating in the same regions.

THE PATIENTS AND DIAGNOSIS OF THE PARASITE SPECIES

1) The patients: All patients were Japanese, except for a Dutch national who was infected in Nigeria and developed the illness in Japan. None of the Japanese patients had been in malaria-endemic areas during the 5-year period before the onset of the current illness, except in the African countries now under consideration.

Department of Public Health, Toho University School of Medicine, 5–21–16 Omori-nishi, Ohta-ku, Tokyo 143, Japan

2) Diagnosis: The diagnosis of *P. ovale* was made by paying particular attention to the morphology of the malaria parasites and of the parasite-infected red blood cells. A 1/50 molar phosphate buffer solution of pH 7.2–7.4 was used to make a Giemsa stain throughout the study period. The main criteria of comparison were: smallness of the *P. ovale* parasite in comparison with that of *P. vivax*, the number of merozoites (average number of merozoites in the mature *P. ovale* schizont being 8) and incomplete separation of merozoites from each other in the mature *P. ovale* schizonts; larger size and smaller number of Schüffner's dots for *P. ovale* in comparison with those of *P. vivax*-infected red blood cells (Wilcox *et al.*, 1954).

3) The country of infection: This could be pinpointed for patients who had stayed in only one country. However, when the patient had stayed in or travelled through two or more countries, the country of infection was designated simply as "tropical Africa".

Results

P. ovale: Twenty-one patients were infected with this parasite in countries south of the Sahara (Table 1). Six patients were infected in Nigeria, 4 in Malawi, 3 in Guinea, 2 cases each in Congo (Brazzaville) and Kenya and one in Tanzania. The country of infection in 3 cases was designated as "tropical African countries" as these patients had stayed in more than 3 countries.

P. vivax: One case each was infected with *P. vivax* in Guinea, Mali and Malawi in sub-Saharan countries and in an island country of Madagascar off the East African coast (Table 1). One patient with vivax malaria who returned to Japan from Kenya could not be confirmed as having been infected there as he had also stayed for some time in India. Two other cases of vivax malaria were infected in Egypt and in Ethiopia, north of the Sahara.

Table 1. Benign tertian malarias infected in Africa (1971-1985)

Country	*P. ovale*	*P. vivax*
North of the Sahara		
Egypt		1
Ethiopia		1
South of the Sahara		
Kenya	2	
Tanzania	1	
Malawi	4	1
Madagascar		1
Guinea	3	1
Nigeria	6	
Mali		1
Congo (Brazzaville)	2	
Tropical Africa*	3	
Total	21	6

* Applied to patients who stayed in or travelled through more than 3 countries.
A patient of vivax malaria who returned from Kenya was excluded as he had stayed in India within 6 months before the onset of the current illness.

Discussion

A high incidence of ovale malaria-about 6% of all of my malaria patients-is indicative of the increasing number of Japanese visiting countries of tropical Africa, on business, construction works, geographical surverys, pleasure, etc. Until 1977–1978, the majority of my malaria patients were infected in Southeast Asia and Oceania rather than in Africa. But the trends have reversed since 1979 when the number of malaria patients infected on the African continent began to surpass that of the patients infected in Southeast Asia and Oceania combined, even though the latter regions are nearer to Japan (Ebisawa, 1982). This tendency was associated with an increasing number of fatal falciparum malaria cases in my series of patients.

Another indication that Japanese are being exposed more to malaria in African countries was the case of a leukemia patient in Japan who contracted ovale malaria following multiple blood transfusions (Amano *et al.*, 1984).

The fact that vivax malaria was endemic simultaneously with ovale malaria in the tropical African countries of Malawi, Guinea and Mali deserves a short comment. *P. vivax* is rarely pathogenic to the black population. The circulation of this species of malaria parasite in the tropical African countries may indicate that it was brought to these areas from other continents by other races such as Arabians, Indians, and other people and was picked up by some local anopheline mosquitoes. The presence of *P. vivax* in Madagascar may be easily understood as there exists anthropologically some ethnical relationship between the people of Madagascar and Indonesia where *P. vivax* is endemic. There have been no reports of a simian malaria parasite which can be regarded as an equivalent to the human *P. vivax* on the African continent, in the way that *P. schwetzi* is regarded as an equivalent to the human *P. ovale* (Coatney, 1971).

References

1) Amano, H., Kurata, S. and Yamamoto, T. (1971): On a rare case of ovale malaria, Nettai, 6, 162–168 (in Japanese)
2) Amano, S., Ohshima, T., Harano, H., Un, Ko-I, Ito, A., Okubo, T., Watanabe, S. and Mouri, T. (1984): On a case of ovale malaria infected by blood transfusion, Japan. J. Trop. Med. Hyg., 13, 189
3) Coatney, G. R. (1971): Simian malarias in man: facts, implications and predictions, Amer. J. Trop. Med. Hyg., 17, 147–155
4) Ebisawa, I. (1982): Recent problems in malaria, in Oda, T. ed. Seminar in Internal Medicine, INF-1, Infectious Diseases, p. 261–271, Nagai Publ. Co., Osaka, Japan (in Japanese)
5) Ebisawa, I. and Komoriya, T. (1972): Case reports of ovale malaria, Naika, 30, 544–546 (in Japanese)
6) Ebisawa, I., Komoriya, T. and Kimura, M. (1973): Study on ovale malaria, J. Japan. Assoc. Infect. Dis., 48, 385–392 (in Japanese)
7) Garnham, P. C. C. (1966): Malaria parasites and other haemosporidia, Blackwell Scientific Publications, Oxford
8) Jeffery, G. M., Young, M. D. and Wilcox, A. (1954): The Donaldson strain of malaria. 1. History and characteristics of the infection, Amer. J. Trop. Med. Hyg., 3, 628–637
9) Jeffery, G. M. and Young, M. D. (1954): The Donaldson strain of malaria. 4. An evaluation and status, Amer. J. Trop. Med. Hyg., 3, 660–664
10) Lysenko, A. J. and Beljaev, A. E. (1969): An analysis of the geographical distribution of *Plasmodium ovale*, Bull. W. H. O., 40, 383–394

11) Report of a WHO Scientific Group (1969): Parasitology of malaria, WHO Technical Report Series No. 433 (Geneva)
12) Wilcox, A., Jeffery, G. M. and Young, M. D. (1954): The Donaldson strain of malaria. 2. Morphology of the erythrocytic parasites, Amer. J. Trop. Med. Hyg., 3, 638–649

アフリカ大陸で感染した良性三日熱型マラリア (*P. ovale* と *P. vivax*)

海老沢　功

アフリカ大陸で感染した三日熱型マラリア27人の内，サハラ砂漠以南の地域で感染した者は25人で，卵型マラリアは21人であった。卵型マラリア原虫は，少数の例外を除き熱帯アフリカにしか流行していないので，この事実は熱帯アフリカに旅行，或いは滞在する日本人が多くなった事を示す。卵型マラリア感染地はナイジェリア，マラウイ，ギニアがそれぞれ6，4，3人で，その他ケニアとコンゴ（ブラザビル）が2人ずつ，タンザニアが1人，西アフリカの3つ以上の国に滞在した者が3人あった。

三日熱マラリア患者は，サハラ砂漠以南の地域では，マラウイ，ギニア，マリおよびマダガスカルで1人ずつ感染している。サハラ砂漠以北ではエジプトとエチオピアで1人ずつ感染している。

特に注目すべき点は，元来黒人にはほとんど病原性がないと言われている三日熱マラリア原虫が，熱帯アフリカの国で卵型マラリア原虫と同時に流行していることである。熱帯アフリカの三日熱マラリア原虫は，おそらくアフリカ大陸以外の地域から，アラビア人，インド人，その他の人種によって持ち込まれたものであろう。マダガスカル島の住民は，インドネシア人と民族学的に近縁であるといわれているので，マダガスカル島に三日熱マラリアがあっても不思議ではない。

熱帯アフリカの国には，三日熱と卵型マラリアが同時に流行しているので，血液標本はpH7.2–7.4の緩衝液を用いて注意深く検査する必要がある。

東邦大学医学部公衆衛生学教室

日本熱帯医学会雑誌　第14巻　第2号　1986　91-114頁

第27回　日本熱帯医学会総会講演抄録（1）

期　日：　昭和60年10月30日（水)—11月1日（金)
会　場：　神戸国際会議場（神戸国際交流会館内)
会　長：　神戸大学医学部教授　松村武男

目　次

特別講演

シンポジウム

佐藤　喜一　（金沢医大・熱帯医研）

5c　無償援助と並行して行う技術協力

鈴木　　守　（群馬大・医・寄生虫）

5d　日本国際救急医療班（JMTDR）の活動について

鵜飼　　卓

（大阪府立千里救命救急センター）

5e　バヌアツ共和国マレクラ島における眼科活動

岩崎和佳子　　（関西医大・眼科）

5f　デング出血熱に関するインドネシアと日本との医学医療協力

船原　芳範　（神戸大・医・一生理）

5g　ネパール・トリブバン大学医学教育プロジェクト

欠田　早苗　　（兵庫医大・二解剖）

岩崎　忠昭　　（兵庫医大・一内科）

5h　フィリピン共和国熱帯医学研究所プロジェクトからみた医学医療協力

布上　　薫　　（九州大・医技短大）

Ⅲ　熱帯地における旅行者感染症

—その現状と対策を中心に—

1　司会のことば

中林　敏夫　　（阪大・微研・原虫）

青木　隆一　　（大阪市立桃山病院）

2　帰国者における感染症の現状

青木　隆一

（大阪市立桃山病院・感染症センター）

3　国際伝染病—ラッサ熱，マールブルグ病，エボラ出血熱—について

今川　八束

（都立墨東病院・感染症科）

4　ウイルス性肝炎について

志方　俊夫　　（日本大・医・病理）

5　細菌性腸管感染症

竹田　美文

（東大・医科研・細菌感染）

6　マラリアについて

高田　季久（大阪市大・医・医動物）

7　治療薬剤からみた熱帯性寄生虫病

尾辻　義人（鹿児島大・医・二内科）

一　般　講　演

（次号掲載予定）

学　生　講　演

懇　話　会

（次々号掲載予定）

特 別 講 演

Ⅰ Dengue hemorrhagic fever: a critical appraisal of current hypotheses

Leon Rosen（ハワイ大）

（英文参照）

Ⅱ 科学技術と国際交流

岡本 道雄（科学技術会議議員）

西洋の科学技術は目覚ましく進歩し発展し，今や世界を制覇してしまった。日本も明治維新以来，西洋から科学技術を導入しこれを工夫し発展させて来た。先ず明治の改革では，科学技術によって武器をつくり，軍国主義をもって世界に乗り出そうとした。次に第二次世界大戦後の改革では，科学技術を企業化することによって，経済的に繁栄し今では世界第２の経済大国になった。しかし歴史的にみて，武力のみでまた経済のみで国際社会に伍して長く栄えた国はないのである。国際社会で信頼される事が大切なのである。その為に日本はどうすればよいのか。私は次の３点が重要だと考える。

第１に，外国人を受け入れることである。人が外国へ行った時は，所詮切り花である。国民はその国で見てもらうことで，本当の理解が得られる。日本人が本当に美しいのは，日本の土においてであり，その土に生えた花がやはり一番美しい。切り花はやはり切り花だけである。その意味でこれからの国際交流というのは，日本に受け入れるという方向に最大の努力をすべきである。そこで政府は今，二十一世紀までに10万人計画というのを立てている。

第２に，日本は今まで世界から科学技術を受け入れてここまで繁栄したのであるから，基礎科学で人類の為になることを積み重ねなくてはいけない。これは単に日本の国益のためだけでなく，基礎科学で世界の為にやるべきことがある。砂漠化を防ぐとか，酸性雨をどうするかと言った地球的な問題になると恐ろしく金がかかり，アメリカか日本でないと出来ない基礎科学がある。そういうものにしっかりと金を出して，世界に報いる事が大事である。

第３は，昔からよく「和魂洋才」という事が言われたが，日本人の魂とは何であるかを，今よく考えてみなければならないという事である。今や西洋の科学技術が人間に直撃して，資源枯渇，自然破壊，公害等の多くの深刻な問題を起こしている。また目には見えない人間の心に，どういう影響をもたらしているかというと，これは計り知れない恐ろしい問題であると考えられる。これを救うのはどうしても東洋の精神だと，西洋では考えられている。なぜなら西洋の科学技術の本質は，自然と人間が対立するところから始まっている。人間の理性だけ働かせて，理性で自然を観察して自然の中の法則を見つけて自然を利用し活用し，さらに征服しようというのが近代科学技術の精神である。ところが東洋の考え方では，自然と人間は対立していないのである。自然の中に人間がいて，人間も動植物も同じく自然であるという考え方である。調和の中にあるのである。この様な精神をもつ日本や東洋を世界は熱い目で見ている。

この点日本という国は，東西の文化の接点であるし，また科学技術の価値を日本人ほど知っている国民はないのである。日本は科学技術で生きて来たのであり，その功を最もよく知ると共に，また原子爆弾を体験し科学技術が誤って使われた時の罪を，これほど知っている国民はないわけであ

る。そういう日本人が「和魂」とは何であるかを今しっかり認識する事が大切である。

日本の世界における立場は大きく変化し，今や日本の内政はまさに日本の外交であり，日本の内部でやっていることは，すぐ日本の外交になっている。その日本の外交は世界の内政，世界政策となっているのである。それくらいの立場に変わっているということの自覚が，日本人一人一人の中にあってこそ，国際交流というものが政府の命令でなく，また政府の政策でなしに国民一人一人の自らのものとして，この時代の科学技術，国際交流の方向が出て来るのだと思う。

シンポジウム

I　熱帯医学と分子疫学

1　司会のことば

石井　明　（岡山大・医・寄生虫）
三舟求真人　（大分医大・微生物）

感染症の制圧に，その病原体の伝播様式や存続様式，あるいは地理的分布等を知るための疫学的研究が不可欠であることには，疑いの余地がない。感染症の疫学はその病原体の種類により多少の違いはあるが，これまで主として血清学的手法によって行われ，幾多の輝かしい業績があげられてきた。しかし，これまでの手法では，病原体株間の詳細な違い，ひいては伝播経路等を詳細に解析するには限界があり，感度の高い新しい手法の導入が待たれていた。

近年，分子生物学分野における新しい発見と技術の開発により，遺伝子の抽出とその塩基配列の決定，制限酵素による遺伝子の切断とその断片の電気泳動法，遺伝子操作による遺伝子のクローニング解析，RNA のオリゴヌクレチオドフィンガープリント法等が容易に行えるようになり，疫学研究にも応用されるようになった。そして，このような分子レベルでの疫学のことを，分子疫学と呼ぶようになった。

分子疫学は，病原体の単純性と取扱いの容易さから現在，ウイルス学および細菌学分野で一歩進んでいるが，原虫，寄生虫分野でも遺伝子レベルでの解析が行われるようになってきた。このシンポジウムでは熱帯地における感染症の主要な病原体である寄生虫，原虫，細菌およびウイルスの各分野において，分子遺伝学的研究，あるいは分子疫学的研究がどのように進められているかについて話題を提供していただき，その現状を把握し，今後の熱帯医学研究の推進に重要な貢献をするであろう，分子疫学の展望を考える機会としたい。

2　蠕虫幼虫の抗原遺伝子の解析

菅根　一男　（横浜市大・医・寄生虫）

蠕虫類，とりわけ線虫類幼虫から抽出した虫体抗原，および幼虫の培養上清より抽出した ES 抗原は，免疫診断上有効で，特に ES 抗原は抗原特異性が高いとされている。なかでも犬回虫幼虫，および旋毛虫幼虫 ES 抗原は幼虫移行症，旋毛虫症の診断に不可欠である。しかし，これらの抗原を一定量得るためには大量の幼虫を採集して培養しなければならない。そこで遺伝子操作の技術を応用して，抗原を大量に採取することを考えている。今回実験に用いたのは旋毛虫感染幼虫で，まずこれらの抗原を分子レベルで解析するために，^{35}S-methionine を加えた培養液中で幼虫を培養した後，培養上清を 30% PEG in 0.9% NaCl 中で濃縮して ES 抗原を，また幼虫を超音波で粉砕して虫体抗原を作製した。そしてそれぞれの抗原に旋毛虫感染マウス血清を加え形成された AgAb complex を，*S. aureus* Cowan 1 株で吸収した後 IgG 抗体と反応する抗原ポリペプタイドを，SDS を加え熱処理して分離した。そして SDS-PAGE autoradiography で抗原ポリペプタイドの解析を行った。その結果，ES 抗原，虫体抗原とも IgG 抗体と特異的に反応する数種類の抗原ポリペプタイドが認められた。特に ES 抗原の 48 Kd のポリペプタイドは，感染血清中の IgG 抗体と強く反応した。次にこれらの抗原の遺伝子レベルでの解析を行うため，液体窒素で凍結した幼虫を Freezer/Mill で粉砕し，可溶成分中より CsCl 超遠心法で RNA 分画を採取した。そしてこの RNA 分画を用いて *in vitro* translation を行い translation products を感染血清と反応させた後，AgAb complex を，*S. aureus* Cowan 1 株で吸収し SDS を加え熱処理した後，SDS-PAGE autoradiography で translation products 中に抗原ポリペプタイドが合成されているか否かを調べた。その結果感染血清

中の IgG 抗体と特異的に反応する 48 Kd の抗原ポリペプタイドが，translation products 中に認められた。すなわち旋毛虫幼虫 mRNA の *in vitro* translation により合成された抗原ポリペプタイドは，ES 抗原中の主要抗原ポリペプタイドと分子量が等しかった。この旋毛虫より抽出した RNA 分画より oligo (dT)-cellulose ゲルカラムにより，poly (A)-rich mRNA を分離した。そしてショ糖密度勾配液を用いた超遠心法により，poly (A)-rich mRNA を分画し，各分画中の mRNA で抗原ポリペプタイドを translation した mRNA を含む分画を採取し，抗原特異的 mRNA を濃縮した。次に細菌を用いて抗原遺伝子の cloning を行うために，*in vitro* でこの mRNA に対応する cDNA を合成した。cDNA の first strand は Buell ら (1978) の方法に従い，second strand は Gubler ら (1983) の方法に従ってそれぞれ合成した。この結果 2 Kb を中心にした cDNA が合成された。

3 最近におけるアフリカ・トリパノソーマ同定法の進展

蛭海　啓行，V. ナントリア，
B. クウクラ，O. オーレ・モヨイ，
P. マジワ
（国際家畜疫病研究所・ケニア）

アフリカ・トリパノソーマ症は住血寄生原虫トリパノソーマに起因し，その主要病原体 (*Trypanosoma brucei brucei, T. b. gambiense, T. b. rhodesiense, T. congolense, T. vivax*) はツェツェバエにより媒介される。本症の診断と病原原虫の同定は，主に形態学的検索と血清学的検定に依存してきたが，精度が低く使用範囲が限定されていた。簡易でしかも精度の高い同定法として，最近 4 つの同定法が新たに開発された。

A．単クローン性抗体法：体外培養法で増殖させた *T. b. brucei, T. congolense,* ならびに *T. vivax* の表面外皮を欠くプロサイクリック型を免疫抗原として種特異単クローン性抗体を調整し，被検トリパノソーマを固定後，その種特異的抗原を免疫螢光抗体法で検定する方法と，サンドイッチ ELISA 法で，被検血清中に溶出している種特異的抗原を検索する方法がある。現段階では，(a) *T. b. brucei, T. b. gambiense, T. b. rhodesiense,* (b) *Nannomonas* 亜属に属する *T. congolense,* と *T. simiae,* ならびに (c) *T. vivax* の 3 グループの識別が可能になっている。

B．アイソエンザイム法：各種トリパノソーマのアラニン・アミノトランスフェラーゼ等，10種以上の酵素を指標として，それぞれの酵素について電気泳動法でスターチ・ゲル，または SDS・ゲルに種特異的アイソエンザイムのパターンを展開し，これらを組み合わせて最終的に種の同定を行う。従来識別が困難であった Brucei グループの 3 亜種を含め，多くの種が同定出来るようになった。しかし，手法が煩雑なため，適用範囲は限定されている。

C．核 DNA 交雑法：*T. b. brucei, T. congolense,* ならびに *T. vivax* の血流型から，それぞれの種に特異的な ^{32}P・リコンビナント・プラスミドを調整し，これを被検トリパノソーマの種特異的 1 本鎖核 DNA と交雑させて同定を行う。現在，(a) *T. b. brucei,* および *T. b. rhodesiense,* (b) *T. b. gambiense,* (c) *T. congolense,* ならびに (d) *T. vivax* の 4 グループの識別が可能である。

D．DNA 分子核型分析法：被検病原体をアガロース・ゲルに包埋し，DNA 以外の成分を酵素で除去した後，パルスフィールド・ゲル電気泳動法 (Carle and Olson, 1984) を用いて「染色体サイズ」の DNA をアガロース・ゲルに展開させ，分子の大きさにより分離した DNA バンドのパターンを基準に種の同定を行う。まだ実験の段階であるが，トリパノソーマ症主要病原原虫 3 種の同定が可能であることが示されている。

従来の同定法に，新方法のいくつかを併用することにより，研究室における実験材料の同定の精度は著しく高められた。しかし，フィールドにおける疫学的調査には技術の簡易性が不可欠なため，上記，特に A および C 同定法の簡易化が現在強力に進められている。

4 毒素原性大腸菌とコレラ菌の分子疫学

山本　達男　（順天堂大・医・細菌）

バングラデシュなどの環境衛生が整っていない発展途上国では，コレラ菌や毒素原性大腸菌は深

刻な乳幼児下痢症の病原体であり，その制圧が重要な課題となっている。この毒素原性大腸菌とコレラ菌の病原性因子の解明のために分子遺伝学的手法が導入され，この分野を先導する幾つかの大きな研究成果が報告された。

1．毒素性大腸菌 (ETEC)

①病原性因子のまとめ：ETECは，菌体表層線毛を介して小腸粘膜上皮細胞に定着，増殖し，腸管毒素を産生して下痢を惹起する。腸管毒素は，易熱性毒素 LT と耐熱性毒素 STI, STII の3群に大別される。

②プラスミドとトランスポゾン：腸管毒素性は Ent と呼ばれるプラスミドに支配される。腸管定着性線毛もプラスミドに支配される場合が多い。STI 遺伝子がレプリコン間を移動可能なトランスポゾンであることが証明されたが，これは細菌病原性トランスポゾンの最初の発見であった。

③腸管定着性線毛：ヒト株の CFA/I とブタ株の K88, K99 等の線毛遺伝子のクローニング解析が進んでいる。

④ST：STI, STII 遺伝子の全塩基配列が決定された。STI の場合，成熟ペプチドは遺伝子産物（前駆体）のC末端に位置する。

2．大腸菌 LT とコレラ毒素

①遺伝子と遺伝子産物：LT とコレラ毒素は，分子性状，作用機序ともに類似し，いずれもサブユニットAとBから成る。このサブユニット遺伝子，およびオペロン構造の全容が明らかにされた。LT とコレラ毒素の相同性は，DNA レベルで78%，アミノ酸レベルで79%である。

②遺伝子の進化：コレラ菌と大腸菌の分岐時間は約6億7千万年前である。また，約1億3千万年前にコレラ毒素遺伝子が，コレラ菌から大腸菌に移り，進化変遷して LT 遺伝子となった遺伝構図が考えられる。

③遺伝子の重複：コレラ菌染色体上に位置するコレラ毒素遺伝子は，繰り返し DNA 配列 (RS1) にはさまれており，RS1 間で起こる recA 依存性の組換えを介して遺伝子の数を増やしたり減らしたりしている。生体内通過は遺伝子の重複（強毒化）を引き起こす。

3．コレラ毒素以外のコレラ菌病原因子

小腸への定着との関連で，赤血球凝集因子と線毛が，毒素として，溶血毒，乳飲みマウステスト陽性因子，PF 因子，志賀毒素類似毒素等が研究されている。溶血毒オペロンの上流に，逆転性 DNA が見いだされた。

4．疫　学

LT, STI, STII, コレラ毒素の各遺伝子をプローブとした，ETEC, コレラ菌，その関連細菌の DNA 診断法が，米国・J. B. Kaper, J. G. Morris, W. K. Maas らのグループで，またタイ・P. Echeverria らのグループで行われている。

5　RNA パターンからみたケニアにおけるロタウイルス感染

千葉　靖男　　(札幌医大・小児科)
宮崎　千秋　　(九州大・医・小児科)

ヒトロタウイルス (HRV) は乳幼児急性胃腸炎の主要な病原体である。また，開発途上国における疫学的検索では，HRV 胃腸炎が乳児死亡の大きな原因であり，小児の保健衛生上，深刻な問題であることが明らかにされている。HRV 感染では激しい下痢，嘔吐が出現し，急激に脱水状態となるため，水分，電解質の補給が必要である。このため，経口輸液剤の実験的投与が各国においてなされているが，有効な HRV ワクチンの開発もまた，今後の重要な課題である。

HRV は11本の分節 RNA をジェノムとして保有しており，その分子量は約 0.2×10^6～2.0×10^6 ダルトンである。糞便中に排出される HRV を精製し，SDS でウイルス粒子を破壊し，フェノールで除蛋白後，エタノールでその RNA を抽出し，PAG 電気泳動を行うと11本の RNA バンドが識別される。また，この電気泳動型は HRV 株により種々の違いがあり，最も顕著で，容易に認別されるのはいわゆる “short”, および “long” type である。前者は HRV subgroup I, serotype 2 の抗原性を有し，後者は subgroup II, serotype 1, 3 または 4 の抗原性を有する。一方，このような HRV RNA の各株における電気泳動度の違いを利用して，分離株の弁別，分布，伝播など疫学的研究をすることができる。

我々は1982年—1983年前半にかけて，ケニアの

2大地区におけるHRV感染をRNAの分析により検討した。海岸地区では，まず，27%（8—45%）の頻度で，胃腸炎乳幼児よりHRVが検出された。その70検体につきRNAの分析を行ったところ，16の違った泳動型が得られ，そのうち，short typeは3パターンであった。ナイロビ地区では30検体より，18の泳動型が得られ，short typeは6パターンであった。なお，これら両地区で共通なものは1パターンのみであった。モンバサを中心とした海岸地区の成績では，ある特定の電気泳動型が時期的に優位を保つ傾向が見られ，また，新たに出現したウイルスにより，それが交代するとともに，周辺地区のHRV流行の原因となっていた。

以上の結果から，人口の密集するケニアの2大都市においては，様々なRNAパターンを呈するHRV感染がendemicに存在し，また，人口密度の低い集落におけるHRV感染は隣接する都市の流行の影響を受けていることが，明らかとなった。当国ではHRV感染は季節を問わず存在し，日本など寒冷地域のそれと異なるが，様々なHRVの存在，およびその出現と，このような疫学的特徴が密接な関係にあるように思われた。ケニアにおけるHRV感染の疫学的研究は，いま，その緒についたばかりであり，最終的な本症のコントロール策の確立のためにもより詳細な検討が必要である。HRV RNAの分析は，このための1つの有効な手段と思われる。

6　オリゴヌクレオチドフィンガープリント法によるゲタウイルスと日本脳炎ウイルスの解析

堀　　博之，森田　公一，五十嵐　章
（長崎大・熱帯医研・ウイルス）

要　約

マレーシアと日本各地の野外にて分離されたゲタウイルス（GETV）およびその変異株と，日本，中国，ベトナム，タイ，シンガポールで分離された日本脳炎ウイルス（JEV）について，オリゴヌクレオチドフィンガープリント法による遺伝子RNA解析を行い，分子疫学的考察を行った。

1，日本で分離されたGETV株間では共通のスポットは多かったが，マレーシアの株との間の共通スポットは少なかった。

2，GETVの野外株　B42，および123Aから，それぞれ得られた変異株P–14とP–15，および123A–15と123A–16はそれぞれ原株に比べ数個のスポット変化を示しこれらの変化は同一ではなかった。

3，同一の蚊乳剤より蚊細胞で分離されたGETVの123A株と，マウス脳で分離された123M株とでは，2個のスポット差を認めた。

4，日本で分離されたJEV株間では共通スポットが多く，またタイで分離された株間でも同様であったが，日本の株とタイの株間では共通スポットは少なかった。

材料と方法

ウイルス：GETVはマレーシアで分離された原株AMM20201と，日本で分離された18株の総計19株。JEVは1935年から1983年まで国内各地で分離された22株と，国外で分離された16株の総計38株である。細胞：ヒトスジシマカ培養細胞クローンC6/36細胞を用いた。方法：GETVでは感染細胞培養液に，^{32}Pを加えRNAを標識し，ウイルスを濃縮精製した後，フェノール法にてRNAを抽出し，RNase–T1にて切断したオリゴヌクレオチドを二次元電気泳動した。JEVでは精製ウイルスRNAをRNase–T1で切断後，^{32}P–ATPとポリヌクレオチドキナーゼでラベルし，二次元電気泳動した。結果は要約の通りである。

考　　察

GETVとJEVは，分離年代，および分離地域が異なる程，共通スポットは少なくなる傾向があり，このことは自然界において，ウイルス遺伝子の変異と選択とが，地理的に充分離れた地域では，それぞれ独立して進行することを示唆するものと考えた。また，GETVの野外分離株では，ウイルス遺伝子の変異により多様化した遺伝子構成を有したものがあり，哺乳類宿主の中で増殖することにより選択されるものと考えた。

ウイルス分与に関し，予研・大谷部長，緒方博士，愛媛大・小林教授，日本中央競馬会・熊埜博士，阪大微生物病研究会，大阪府立公衆衛生研究所に深謝いたします。

Ⅱ　熱帯諸国と日本の医学

1　司会のことば

深井孝之助　（阪大・微生物病研究会）
坪井　誠吉　（神戸大・医・医学研究国際交流センター）

現在我々が営んでいる健康かつ安全な生活を，世界中の人々全てが享受している訳ではないこと，むしろ途上国の大半の人々はそれを享受することができないことを我々は知識として知っている。この隔差を生む原因の大きなものの一つが病気であり，貧窮と病気との悪循環は今も絶ち切ることができない。この隔差は放置すれば拡大し続ける一方であり，各国間の緊張を生み，不安定な国際関係にまで立ち至ってしまう。

貧困の大因である病気を制圧するにはいかにすればよいのか，それについて先進国，就中日本が何をしなければならないのかが，各演者によって論じられることになる。

その柱となるものは，人材養成，必要な，特に途上国の現状に密接した技術の移転，および資・器材の供給であり，その為の多岐にわたる現在の強力実施方式それぞれの評価が論じられることになろう。

更に途上国と医療協力がその国の現状や，他の種々の協力とよく整合されたものとして実施されなければ，途上国における組織的な保健向上にはつながらず，その為の方略はいかに考えられるべきかも，論じられねばならない重要な点である。

世界保健機構は世界的視点に立つ「西暦2000年までに全ての人に健康を」を目標として具体的方策の実施にふみ出し，その前段階として1990年を目途に世界の子供達のための免疫拡大計画（EIP）を推進している。この流れの中でわが国が寄与しうるのはいかなる点であろうか？

一方物質に支えられた先進諸国の文明は，より素朴な精神文化にささえられる途上国の社会を圧しつぶしかねないように見える。国際協力に於いて，特に医療協力に於いて，この様な傾向を是正すべく熟慮の上で協力計画が進めなければならないと考えるが，この「心」の問題に関して我々の反省は十分であろうか。

途上国が医療協力について求める根底には，基本的な人間としての要求を満たすために，いかに国民のための医療を確立するかの命題がある。この基本的な命題を見きわめてわが国の途上国に対する医療あるいは医学の協力が進められ，我々が思いこみや，単なる学術的興味のみに支えられて行動しているのではないことも確認したい。

幸いにしてここに，我々は途上国の方々から直接に意見をうかがう機会を持つ。批判があればそれに耳を傾けるだけではなく，率直にこれを我々の行動に生かすことが，今必要なのであり，また途上国の方々が控えめに語られであろうことの言外の意味を理解できるよう，我々自身を高めることに努めたい。

途上国との医療協力は，医学に携わる誰もがその心の中に堅持している人道精神に基づいて，人間としてなさねばならない仕事である。そしてそれは全世界のための安全保障策として我々の手の中にある。このことをこの機会に自ら確認できれば幸甚である。

2　海外医学医療協力のあり方

2a　海外医学医療協力における問題点

林　　滋生　（予研）

医学医療における近年の進展はまことに目覚ましいものがあり，わが国においては，たとえ必ずしも完全ではないにしてもその恩恵を十分に享受してきていることは万人の認めることであろう。平均余命の著しい延長により今や世界一の長寿国の地位を得るにいたったことは，その1つの現れとみることができる。

この恩恵は当然のことながら発展途上国にも及ぼされるべきものであるし，現実に国または民間の各機関，あるいは個人ベースですでに海外医療協力の努力がなされていることは多数の事例が示している通りである。しかしながら他の先進諸国に較べると日本の海外援助における歴史はまだ短

く，経験不足の故に，それぞれの場で困難に直面し，必ずしも所期の目的をあげることが出来ない場合も決して少なくはないようである。これらの問題点の解決は1つにかかって多くの経験を積むこと以外にないと思われるが，各方面の実施における経験を持ち寄り，情報を収集交換する事が甚だ有効であり，1983年大阪で開かれた第21会日本医学会総会で国際医療協力のシンポジウムがもたれのを契機として，その後誕生した国際協力サロンが頻繁にそのような場を設営し，成果を挙げつつあることは同慶に堪えない次第である。

医学医療の面での国際協力は，本来発展途上国においてそれぞれ，自らの保健医療の進歩向上を，自らの手で行えるようにするための必要な援助をなすことであって，その根幹は技術移転であり，それを通じてその国に必要な人材の養成とシステムを創ることにあると思われる。

上記の目標達成には実はかなりの年月を要するのが通常でり，円滑に有効な技術移転を行う為には考慮しなければならないいくつかの重要な問題点がある。たとえば，1) 受入れ国におけるその技術の必要性と重要度，2) 受入れ能力の度合，3) 受入れた技術を活用し得るシステムの有無とその効率，などであろう。これらの考慮のうえで移転すべき適切な技術が選定されたなら，さらにこれを如何に有効適切に移転し得るかの問題点を解決しなければならない。通常行われる専門家の派遣，研修員の受入れ，必要機材，施設の供与等，ならびにこれらの組合せによるプロジェクト方式があるが，このいずれの面においても多くの困難を克服しなければならないことは，既に経験が示す通りである。

しかしここではさらに，別の事項として考慮しておくべき事があることを指摘しておきたい。それは広く援助ということに関わる基本的なことであるが，医療協力の場合においても，医療協力のある1つの技術を移転するだけでは，問題が片付かないことがしばしばである。オンコセルカ症の対策として有効であったダムの建設が，マラリアの媒介蚊の発生水域を作り出したりというように，1つの問題の解決が別な問題を生み出すこともあるし，医療協力のみならず，農業あるいは他の社会経済開発計画との関連を考慮しなければ，適切な効果のあがる援助とはなりえない場合がある。

なお上記の長期的展望にたつ援助と異なる短期あるいは緊急時の医療協力も存在し，これはまた別個の異なる問題を包蔵しているが，別の機会にゆずりたい。

2b 医学研究国際交流センターの活動と理念

岩井　誠三　　(神戸大・医・医学研究国際交流センター)

医学研究国際交流センターが学術審議会の答申の主旨に沿って，発展途上国との学術交流をはじめて以来，満7年を経過しようとしている。そこで，我々が実施してきた交流の理念と実状を報告し，参考に供したい。

本交流の主旨は，対象国における研究者の育成であり，これによって各国国民の健康と福祉の将来的向上に役立てることにあるが，同時にわが国の研究者が対象国の実情を目の当たりにし，その生活・文化への理解を深め，医学研究を介して将来にわたる有効と信頼の絆を強めて，平和に寄与することにあると考えている。

医学の研究は極めて広汎にわたり発展を遂げつつあるが，本来の使命である疾病の克服と健康増進のため，限られた予算のなかで，可能な限り早期に目的を達成していく為には，単なる高度の技術や先端知識の導入ではなく，それぞれの対象国において早急に解決すべき医学・医療上の課題のなかから，双方が共同研究として取り上げ，その問題解決の過程において相互に研究者の交流による育成をはかることが最も好ましい方法と考えている。

現在までにインドネシア，フィリピン，タイに加えてシンガポールを対象として，各国に固有な問題，あるいは共通した10に及ぶ共同研究課題を選択し，18の国内協力大学ならびに，14名の協力研究者の絶大な協力を得て，実効のある交流を続けてきた。この間に交流し得た研究者，延総数は523名に及び，対象国数の増加とあわせ年度毎に着実に増加してきた。各対象国における研究者交流数の実態を年度毎にみると，当初は現地の実状を調査する目的から派遣研究者数が受け入れ研究

者数を大きく上回っていたが，研究の進展とともにほぼ同数となってきている。受け入れ研究者の年齢分布を解析すると，前述のように本交流の主旨が対象国における研究者の育成と将来的発展を期待するものであるため，当初は当時指導的立場にあった研究者が，自国における将来的展望を構築する資料を得る目的と，わが国の実情視察に来日する例が多く，年齢的にも40歳以上が多かったが，最近では次代の研究教育の担い手である30代，40代研究者が大半を占めるようになった。このことは，交流事業の主旨が対象国において充分に理解されていることを物語ると同時に，わが国との交流が有意義であると受けとめられた証拠と理解し，喜んでいる。本交流予算の年度増加率を見ると，最近国家財政の緊縮を求められているなかで，着実な増加を示してきた。このことは所轄官庁関係者が本交流事業の意義を十分に理解され，同時に医学領域における実績を評価されたものと受けとめ，その配慮に感謝すると同時に，センターの責任の大きさを痛感している。

当センターが現在まで歩んできた7年間は，人材育成のための有効な具体策を模索してきた期間であり，多くの問題点を抽出することが出来た。特に各種の条件を異にする多数国を対象として，その目的を達成していく為には，交流課題の拡大を必要とするが，双方に人員，機材ならびに経費上多くの制約があり，また現在まで育成してきた多くの萌芽研究者に対する物心両面にわたる支援が必ずしも充分とはいえず，今後に残された大きな課題を考えている。

3　アジアから見た日本の医学

Domingo E. O.　（フィリピン大）
Sujudi　（インドネシア大）

（英文参照）

4　国際協力機関の医学医療協力

4a　国際協力事業団（JICA）の熱帯病に関する協力活動

長谷川　豊
（国際協力事業団医療協力部）

はじめに：JICAの保健医療協力プロジェクトは，昭和60年7月現在34で，1つのプロジェクトの中に種々の要素を含む総合的プロジェクトもあるが，大凡の分類を行うと，熱帯病関係 7，消化器疾患 4，地域保健 4，家族計画 4，母性・小児疾患 3，製薬・ワクチン 3，看護教育 2，総合病院プロジェクト 2，医学教育，結核，循環器疾患，臨床・衛生検査，核酸・免疫学が各1となっており，熱帯病関係プロジェクトが比較的多い。

また，熱帯病プロジェクトでなくても，殆どすべてのJICAプロジェクトは，開発途上国の熱帯地域で実施されており，多数の日本人専門家（医療関係に限らず）をそのような地域に派遣しているので，熱帯病を無視しては，JICAの事業は成立し得ない。従って，これら不健康地への長期専門家については，休暇や健康管理旅行等につき特別の措置を講じているところである。

JICAの途上国への協力の主要形態は，いわゆるプロジェクト方式技術協力と言われる方式であって，これは，途上国の要請に基づき，日本人専門家の派遣，途上国からの研修員の日本での研修，プロジェクトに必要な機材の供与，という3つの要素を有機的に組み合わせて，数年間にわたって協力する方式である。

保健医療技術協力プロジェクトの昭和59年度の実績は，次の通りであった。

	医療協力(計)	熱帯病関係
プロジェクト数	34	7 (21%)
専門家派遣（人）	366	64 (17%)
研修員受入（人）	130	17 (13%)
機材供与（億円）	21	2 (10%)

医療協力部では，マラリア対策協力を強化するほか，ワクチンによる感染症対策の推進について検討をすすめているところである。

熱帯病プロジェクトの紹介：

1.　フィリピン熱帯医学研究所プロジェクト

これは，わが国の無償資金協力（18億円）によりマニラに建設された熱帯病研究所において，マラリア，デング熱等の熱帯病を含む各種感染症の研究能力，検査技術の向上に協力している。

2. タイ国立衛生研究所（NIH）プロジェクト

無償資金協力（約40億円）により建設中のNIHにおいてタイに流行している熱帯病を含む感染症の研究能力の向上，および生物製剤開発への技術協力を本年8月から5年間行うものである。

3. ガーナ・ガーナ大学プロジェクト

ガーナ大学に野口研究所を無償資金協力（20億円）で建設，黄熱病などの熱帯病を含む各種感染症の研究能力の向上に17年以上にわたり協力中。

4. ナイジェリア・ジョス大学プロジェクト

ナイジェリア国中央部プラトー州における熱帯病を含む各種感染症，地方病等につき，ジョス大学医学部の研究能力向上に協力している。

5. ケニア・中央医学研究所プロジェクト

無償資金協力（27億円）により建設された中央医学研究所における熱帯病を含む各種感染症の研究能力の向上のため本年より5年間協力の予定。

6. パラグアイ厚生省中央研究所プロジェクト

中央研究所におけるシャーガス病，リーシュマニア症等，各種熱帯感染症の研究能力向上に協力中。

7. ブラジル・ペルナンブコ大学免疫病理センタープロジェクト

住血吸虫，シャーガス，リーシュマニア，フィラリア症等熱帯病の研究，対策についての協力。

4b 南北問題からみた世界保健機構と日本

蟻田　功　（国立熊本病院）

連日の新聞紙上にアフリカの飢餓が報ぜられているが，これはアフリカを含む発展途上国の政治経済，および保健の深刻な危機状況の片鱗を示すものである。保健医療の面ではこの危機は先進国と発展途上国の増大する，健康格差として理解される。

国際医療協力とはこの南北の健康格差を縮小するため先進国の人的，および物的資源をフルに活用しようとするものであり，世界保健機構（WHO）は，この国際医療協力を強力に推進するフォーカルポイントである。

その活動を理解するためにWHOによる3つの地球規模の事業をのべた。1）天然痘根絶対策事業：1967年WHOはその対策強化をWHOジュネーブ本部に対策本部を設立することにより開始，1980年には根絶宣言を行った。その結果全世界が種痘，および検疫事業を廃止することができた。この成功の重要な教訓は，人類は，政治，宗教，人種の違いをこえて，一つの重篤な疾病を地球から抹殺することができるということを現実に示した点であろう。2）拡大予防接種計画：1979年頃から天然痘根絶計画に従事した多数のWHOの対策員がこの事業にその経験を生かして参加し，結核，小児麻痺，麻疹，破傷風，百日咳そしてジフテリアの6つの予防接種をWHOの協調のもとで，先進国の人的物的資源を投入，1990年までに途上国の子供80%に，普及したいというものである。3）熱帯病研究訓練計画：途上国33億人世界の人口の約3/4のうち，8億人は，マラリア，リーシュマニア，住血吸虫症，睡眠病，フィラリア，又は癩のいずれか一つ，又は二つ以上の疾患に罹患していると推定される。先進国では以上の患者は存在しない。一方，途上国ではその予防や治療の研究をやる能力も資源もなく，これらの疾病が蔓延するにまかせていた。1977年頃よりWHOは世界銀行や，先進国からの寄付をつのって，これらの熱帯病の治療，予防研究を促進している。マラリアワクチンの開発などは，最重要項目であろう。

WHOの活動は，これらのプログラム以外にも勿論，予防，治療製剤の標準化，添加物の規制，成人病対策の方針樹立など多岐にわたっているが，特記すべきこととして，以上の地球規模の対策を総合するものとしてHealth for All by 2000（HFA）という総合対策を1979年に，WHO総会で議決した。極めて野心的な計画であり，2000年まで，あと15年しか残されていない現在どこまで，このHFA計画が成功するか，大いに危惧されるところである。しかしながらアフリカの危機にみられるような南北の健康格差問題を考える場合，日本を含めた先進国はHFAが非現実的だとかいう批判をするよりも，むしろその崇高な精神をくみと

り，途上国援助にできる限りの資源を投入すべきであろう。日本の国際医療協力に対する貢献は，1984年のWHOの予算ではアメリカ，およびソ連についで第3位となっているように，ここ10年間に著しく増大した。しかし先進国中，途上国向けの援助のGNP比はいまだ11位とその順位は低い。しかし，10月24日国連総会における中曽根総理の演説のように，日本の国際協力費は1992年，即ち7年間に倍増する（約400億ドル）予定であり，資金面では日本の貢献度は，将来著しく高まるであろう。

さて，ではそのような増加しつつある国際協力費を，日本は，国際保健医療面で，どのように効果的にまた能率的に使って，国際協力に貢献できるであろうか。まず第1に，天然痘根絶事業の成功にみられるように，予防が如何に治療よりも安あがりであるかということに注目すべきである。天然痘根絶に使用した全世界の費用は，1967年より1980年の根絶宣言まで，3億ドルにしかすぎず，その額は米国における心臓バイパス手術の2カ月分だといわれる。また根絶により，全世界は種痘事業の廃止，検疫事業の削減，種痘副作用の皆無など，全世界の節約額は年間10億ドルといわれる。従って，日本の国際協力は，予防にその主力をおくべきだと考えられる。現在日本の医療保健国際協力費の半分以上が，病院建設や，研究所の設置に偏しているのは，早急に改善すべきであろう。日本は最近バイオテクノロジーの分野で急速の進歩をとげたが，これらの技術を使い，途上国に対するワクチン製造，品質管理，コールド・チェインの樹立など各方面で貢献できるであろう。また日本は，結核対策において過去40年間に，めざましい成功例をもっている。このことは当時の結核療養のベッドの70%が，一般病院ベッドと現在切り換っていることからもわかる。この対策は，サーベイランス，診断，治療，BCG接種，および疫学研究の総合的な施策により成功したものであるが，これらの対策を途上国に国際協力として日本からの人的，および物的の資源の供給を通じて，途上国に導入すれば，大きな成果が期待されるであろう。第2に日本からの保健医療の国際協力で，二国間協定によるものが大きな比重を占めるが，この計画，実施および評価に，是非WHOを介入させることが必要だと考えられる。WHOの豊富な経験および知識は，二国間協定によるプログラムをより強化することは間違いないからである。

4c　東南アジア諸国との医学の交流

酒井　文徳　　（日本学術振興会）

日本学術振興会（JSPS）は世界28カ国とすべての分野の学術交流を実施しているが，ここでは特にアジアにおける医学の交流の実態と，将来に向けての展望を簡単にのべた。JSPSの目的は人材養成であり，施設，研究費に対する援助，協力は行ってはいない。実施しているプログラムの主なものは，1）研究者交流，2）セミナー，共同研究，3）論文博士号取得希望者に対する援助等である。

アジア地域の諸国との交流型式は2大別出来る。1の型は中国，インド，韓国等と行っている型式であり，2国間で協定を締結し，費用を相互に分担し合う型式であり，JSPSが世界各国と行っている通常の型式のものである。東南アジア5カ国（タイ，インドネシア，フィリピン，マレーシア，シンガポール）と行っている型式は一般の型と異なり，殆どすべての費用をJSPSが負担するものである。もちろんこの後者の場合も各国のagenciesとそれぞれ協議し，その課題を選択する方法をとっている。

1）　東南アジア諸国との研究者交流：1982年度の交流数をみると（マレーシア，シンガポールは初期のため統計から省いた）受け入れた医学研究者は40名であり，日本からこれらの国を訪れた研究者は33名であった。同年の米国からの受け入れ数（35名），ヨーロッパ諸国からの受け入れ数（45名）とほぼ同数である。この受け入れ数は年々増加の傾向を示している。

2）　セミナー，共同研究：これらは主として神戸大学が中心となり実施されており，東南アジア諸国以外からの参加者も増加している。

3）　論文博士号取得希望者への援助：わが国における論文博士制度を利用し，日本の大学で学位を取得する希望のある研究者を援助する制度であ

る。日本の学位授与権のある大学の教官を指導者として選び，年に1回程度日本を短期間（2—3カ月）訪問し，指導を受け，母国で研究を継続し，5年以内に論文を完成し，日本の大学に論文を提出し，博士号を取得する制度である。この際の日本訪問の旅費・滞在費はJSPSが負担することになる。現在この制度で援助を受けている医学関係者は12名である。中国，韓国，インドから1981年に受け入れた医学関係者は12名であった。

展望：さきにのべた単なる研究者交流数は，そのプログラムの全体を正確に表現はしていない。何名の研究者がどの程度の日数滞在したのが不明である。最近，特に若手の研究者に比較的長期間（約1年）滞在し，協同研究を行いたいとの希望が増加しつつある。これらの要望に注目する必要がある。広い意味での医学の進歩は，単なる医療技術の習得のみでは達せられない。工学，理学，農学および社会人文領域等を含む広い科学との調和のとれた発展の上にこそ，医学の進歩が期待される。したがって医学のみならず，他の科学の調和のとれた振興を計るべきである。またこれらの科学の推進には，その国に根ざした人々の活動に待たねばならない。単なる経済援助のみではその目的は達せられず，人材養成にウェイトを置く必要がある。東南アジア諸国には日本に期待するところが増大しつつあるが，我々も協力の本質をよく理解し，その要求に効率よく応えたいものである。

5　熱帯諸国との医学医療協力

5a　司会のことば

藤岡　晨宏　　（県立尼崎病院）
辻　　守康　　（広島大・医・寄生虫）

熱帯諸国との国際協力関係を実施する上において，医学あるいは医療面の占める位置は大きいと思う。しかし言語・習慣の異なる外国でこれら住民に密着した医学・医療協力をスムーズに進めるためには，各国の実状に合わせた形で行うことが必要である。

今回の演者の先生方は東南アジア，中南米，アフリカなどの熱帯諸国で，それぞれ実際に活躍された経験をお持ちの先生方であり，各国の医学・医療レベルを目のあたりにされ，身をもって体験された方々ばかりである。比較的医療機関あるいは研究機関の整っている東南アジアや中南米諸国から，殆ど他国の援助依存傾向の強い一部のアフリカ諸国まで，問題となる疾病構造も異なると思われる。

短い時間ですべてを話して戴くと共に，それぞれの問題点を指摘して戴いて，今後の協力関係を進める上で役立たせることが出来れば幸せだと思う。

5b　熱帯諸国との医学医療協力

佐藤　喜一　　（金沢医大・熱帯医研）

一般論ではあるが，熱帯地域の医学医療協力に積極的に参加する手段として，(1)当該国へ赴任し直接協力す場合と，(2)当該国の人を日本へ招いて協力する場合の2つがある。前者の場合は，単数または少数の赴任者対多数の当該国人の関係となるために，言葉の問題を含め，想像以上の努力が要求される。後者の場合は，むしろ逆の関係となるが，多少の問題は周囲の人で補うことができ，これまでに比較的良い評価を得ている。

一方，協力関係の過程は社会的，ならびに経済的制約の影響から避けることが出来ず，例えば(1)の場合は「物のない所」「貧しさの中」での仕事であり，時には古いものや廃用品を再利用したり，代用品を使用する場合も起こりうる。これに対し，(2)の場合には豊富なものの中での協力だけに折角修得した技術や知識が帰国後，有効に応用できるかどうかの不安になり，結果的には器材要請という形ではね返ってくる事がある。

この様に，いずれの方法にも利点や欠点があり，満足な医学医療協力関係をつくりだすことは困難のようである。演者は，上記の2つの場合を経験し，また現在も努力し実行しているので，いくつかの事例を紹介したい。

1)　ラッサ熱の患者の病理解剖（1974)：原因不明の高熱で死亡した29歳のドイツ人医師の剖検例である（Japan. J. Trop. Med. Hyg., Vol. 10, 1982)。JICAの要請でナイジェリア大学の病理解剖学教室へ出向中に，周囲のスタッフの反対に逆らって行った。その結果，大学全体のスタッフか

ら敬愛され，その後の業務に協力的になった。

2) タイ国の無医村での耳手術キャンプ(1981—現在)：タイ国の村や部落で中耳炎患者の耳手術を手伝っているボランティア活動である。当該大学がJICAの協力を申請している。タイ国の耳鼻科医会（約200人）が理解と協力を示している。

3) ヤルシイ医大（ジャカルタ市）と熱帯医学に関する合同シンポジウム（1983—現在)：各年毎に主題を選び，本学から演者を派遣し，発表と討論の機会を作っている。発表した内容を論文としてまとめている。

4) ヤルシイ医大との交流（1983—現在)：(1)演者が客員教授として集中講義のために出向している。(2)ヤルシイ医大のスタッフを大学院院生として受け入れ，研究活動を指導し援助している。テーマはデング熱ウイルスと蚊の虫刺創の実態である。

5c 無償援助と並行して行う技術協力

鈴木　守　（群馬大・医・寄生虫）

わが国が行ったマラリア対策のための無償援助は，6カ国に及んでいる。無償援助は，もともと，単年度予算により建物や施設などを現地に供与する大型援助方式であり，GNPが一定水準に達しない国が援助をうける資格がある。こうした大型援助の1つにマラリア対策援助が組入れられたため，問題点の整理が必要となり，専門委員会の報告書が，59年9月にまとめられた。この報告書の中で，マラリア対策援助に関しては，無償援助と技術援助との協調をはかることが，必要不可欠である事が結論された。技術協力をすすめるためには，現地に日本から派遣された専門家が常時駐在して，現地側専門家と共同作業をすすめることが必要となる。さらに，技術協力の正式な発足までに，双方で整えるべき数々の条件の設定など，相当の時間と労力が要求されるものと想定される。我々は，今までに，ハイチ，スーダン2カ国におけるマラリア対策援助に実際に参加する機会を与えられた。そうした折を利用して，マラリア対策無償援助実施後の技術協力を，限られた人材と時間を利用して，現に存在するカテゴリーのなかで，いかに活用すれば実効をあげることができるかについていくらかの工夫を試みた。ハイチ，スーダン両国とも，無償援助に係わる要請として，小規模な実験室を設営し，間接螢光抗体法，マラリア薬剤耐性試験などを現地側で行う体制を整えたい旨の，申し出があった。この要請をうけて，援助実施に際し，螢光顕微鏡をはじめとするいくつかの実験室機材が現地に送付された。現地における機材の設営に際し，日本側は，現地政府の要請に基づき専門家を1カ月派遣する事を承諾した。派遣専門家として再び現地に赴いた我々は，そこで実験室機材の設営に従事し，同時に技術講習会をひらいて，実験器材の取り扱い，実際に現場での材料の採取，およびその材料を使っての実技指導を行った。その後さらに現地側から研修の要請がよせられたので，研修員として来日した現地技術者に対して技術指導を行った。この様に無償援助に伴う現地調査，専門家派遣，研修事業など既存のカテゴリーを組み合わせて，現地との技術協力を進めれば，小規模な寄生虫学教室においても比較的気軽に無償援助と技術協力の組み合わせを推進させる事が可能であり，現地側の技能が一定の水準に達すれば，共同研究も可能である。こうした共同研究の推進のためには，日本で開発された独自にして現地に適応可能な技法を，確立させていくことが必要である。現在我々は，薬剤耐性試験に関する新しい技法を開発中である。この新技術の野外応用性を現場で検討することなどは，こうした共同研究の好例となる事と考える。

5d 日本国際救急医療班（JMTDR）の活動について

鵜飼　卓
（大阪府立千里救命救急センター）

国際医療協力にも極めて緊急性の高いもの(acute)と，できるだけ早く対応すべきもの(subacute)，腰を落ち着けて取り組むべきもの(chronic)とがある。従来の日本の国際医療協力は，殆どchronicのものに集中しており，acuteのものには全くといってよいほど無力であった。演者らはacute phaseの国際医療協力を模索して日本国際救急医療班（Japan Medical Team for Di-

saster Relief, JMTDR）の組織作りにかかってきたのでその経験を通して学びつつあることを述べた。この組織は，多数のカンボジア難民が極めて悲惨な状況に追い込まれたとき，アジアで生じた悲劇にも拘らず，日本からの救援医療が諸外国に全く遅れをとってしまったことの反省に始まった。すなわち，海外で大災害が生じて救援医療班の派遣が望まれたとき，すぐさまその状況に応じて救援医療班を派遣し得るように準備しようというもので，外務省経済協力局にその事務局を置き，文部省，厚生省，日本医師会，日本赤十字社，日本救急医学会が運営委員会を組織して，その円滑な活動を支えており，医師や，看護婦，調整員など志のある者を予め登録させている。昭和60年９月末現在261名が登録を済ませた。日常活動として，①ボランティアの登録，②携行資器材，医薬品の備蓄，③研修会開催，④ニュースレター刊行，⑤緊急医療協力に関する情報収集などを行っている。

1984年11月，安倍外務大臣のアフリカ３国歴訪に本多憲児 JMTDR 委員長らが同行して，エチオピアの旱魃被災民の状況を視察し，その報告に従って JMTDR のエチオピアへの派遣が決定された。演者は第１次チーム団長として，同年12月10日に成田を立ってエチオピア北部のチグレイ州メケレ地区に派遣され，当時建設中であった被災民キャンプ（人口約２万人）で，エチオピア人医師らを助けて医療活動を行った。以後４次に亙り計32人の医療要員がここに派遣され，当初１日平均30名も出ていた死亡者を４カ月後には０ないし１名に減少させ，エチオピア側にすべての医療品や資器材を引き渡して撤退した。

JMTDR はまた，1985年９月19日早朝メキシコ市を襲った大地震に際しても出動したが，この２回の出動を経験して，①国際的な救急医療協力には団員や物資を運ぶ適切な輸送手段（航空機を含め）を確保することが極めて重要であること，②迅速に現場に到着しなければ無意味であり，地震などの自然災害では24—48時間が限度であること，③医療だけに限定せず，より広範な救助要員や体制が必要であること，④登録者を更に増加させて対応能力を強化する必要があること，⑤上記の目的を円滑に遂行するためには，予めアジアの国々と JMTDR の派遣に関する事前協定を締結するのが望ましいことなどを学んだ。

5e　バヌアツ共和国マレクラ島における眼科活動

岩崎和佳子　　（関西医大・眼科）

1984年以降年２回，今年で合計４回，バヌアツ共和国マレクラ島の眼科医療サービスを行って来た。

同国は80余島を集め，1980年に英仏より独立し，全人口約12万人の内，第２番目に大きな島のマレクラ島（3,500 km^2）には約17,000人が住んでおり，40余りの部落が点在し，医療サービスは，90床の Norsup 病院と40床の Lamp 病院がある。

この下部組織としては６カ所の Health Center と11カ所の Dispensary が主としてプライマリーケアーを担当している。

しかし同国には眼科専門医が全くいないので，年１回オーストラリアから来る眼科チーム（眼科医と眼鏡士のグループ）が１週間に渡って，主な２～３の島の巡回サービスを行っているのみである。

我々は当初より，失明予防に力を入れ，白内障の開眼手術においても，入院から退院迄の管理が充分出来るように１カ所に最低でも１週間の割合で滞在し，術後サービスとしては白内障手術の矯正視力を取り，次回の検診時にその補正眼鏡を持参し，患者に渡す事をルーチンとしている。

1985年７月迄に島民の人口の約12%に当たる2,015名の検診，診療を行い，その時1,382名の68.6%に何らかの眼疾患を認めた。

小学校検診は18校の内16校1,453名の検診を終了し，病院外来で368名，こちらから出向いての地区検診では194名の診察をした。

疾患の主なものとして老視6.5%，トラコーマの疑い5.5%，結膜炎5.4%，白内障4.6%，翼状片3.0%などがあり，紫外線による影響と考えられる白内障や翼状片が多いのが特徴であった。

手術例と白内障15例16眼，翼状片18例20眼であり，特に白内障の場合は両眼視0.1以下で，本人の希望があった人の片眼のみ行っている。

この国には眼科サービスがなく，従って眼鏡の

流通機構も全くないので，視力補正には日本から寄付による眼鏡を持参し渡している。

学校検診では視力1.0以上が95%いて，日本の約30%とは比較にならない位によい視力であった。

一方トラコーマの疑いのある児童が全体の12%(150名) もいて，学校差もあるが2～27%の範囲に患者が広がっていた。この児童にはWHOでも指導している，テトラサイクリン系，エリスロマイシン系の点眼薬，軟膏を渡し始療を開始している。一方1985年10月より学校の先生に眼保健教育として，トラコーマ予防の教育をスライドと文面を作り開始し，コピーを保健省にも提供した。過去の日本でもそうであった様に，トラコーマの撲滅運動は個人の生活水準の向上が第1であり，それには政治の力が絶対に必要であるが，国策上の問題もあるので資料の提供を現在している。

今後は年2回の直接医療サービスと同時に，眼保健教育も同時にしていかなければ，医療協力にはつながらないと考えている。

また地区の検診でも交通機関の問題と合まって，日本の地域医療計画を作る上でも，計画的にこの国で実践する事が上手にいけば，逆にそのノウハウを輸入してみる事も必要である。

今後は今でも物好きといわれているボランティア活動が，1つの専門職として日本の社会に新しい土壌が作り上げられる様に，少しでも努力していくつもりである。

5f デング出血熱に関するインドネシアと日本との医学医療協力

船原　芳範　　(神戸大・医・一生理)

インドネシアとの医学医療協力に関する私達のプロジェクトは，文部省，日本学術振興会，国際協力事業団，神戸大学，インドネシア国教育文化省高等教育総局などからの援助を受け組織され，デング出血熱の出血素因を明らかにし，治療方法を確立することを目的としたものである。このプロジェクトはインドネシア大学と神戸大学が中心となり，1979年に開始され，現在に至っている。この間に得られた成果は，1. The First ICMR Ceminar on Dengue and Dengue Hemorrhagic Fever (Nov. 21–22, 1980 Kobe, Japan)，2. The International Symposium on Disseminated Intravascular Coagulation (Nov. 26–28, 1981 Tokyo, Japan)，3. The International Conference on Dengue/ Dengue Hemorrhagic Fever (Sept. 1–3, 1983 Kuala Lumpur, Malaysia)，4. The First International Seminar on Dengue Hemorrhagic Fever in the Americas (June 15–16, 1985 San Juan, Puerto Rico) 等の国際会議で船原等により発表され，1986年には，これらの研究成果を基礎にし，ASEAN諸国でデング出血熱の治療に関する共同研究が開始されようとしている。

このプロジェクトは，成功しているとみなすことができる。その理由は，7年間継続しているこのプロジェクトを中止しようとする気配すら認められず，両国が中心になってプロジェクトをASEAN諸国にまで拡大しようとしている点にある。

両国から，小児科学，血液学，ウイルス学，免疫学の専門家が参加した私達のプロジェクトの特徴の第一は，自分の専門分野を相互に教授することに最大の努力をしている点で，教授内容はデング出血熱に直接関係するものに限定されず，インドネシア大学病院で日本側の医師は，教科書でのみ知っていた症例を体験することもできた。時には教授する立場になり，また時には教授されるという関係から相互に信頼できる人間関係が生じ，プロジェクトが長時間継続していると考えられる。

第二の特徴は，患者から得られた標本の検索は，インドネシア大学で行うという点で，その結果プロジェクトに直接参加していない研究者達にも検査手技等の実習が可能になり，より大きい教育効果を得た。尚，インドネシアでの研究遂行に関しては，インドネシア大学側の配慮および国際協力事業団等の好意により研究室を作り，種々の測定機器等を設置することができた。又，インドネシア側研究者の3名が，日本学術振興会の援助により日本で研究を継続でき，その内の2名は論博コースの研究者として毎年3—6カ月日本に滞在し，研究できたこともプロジェクト遂行の利点になった。彼らの得た研究成果は，インドネシアでのデング出血熱研究に直結し，また彼らが若い研究者を教育できたため，日本側からの参加者が少

数であっても，試薬などがあれば，プロジェクトを遂行することが可能になってきた。

この様に，種々関係機関の御好意により，我々のプロジェクトは総合的には非常に良い結果を生み，益々発展しようとしている。

5g ネパール・トリブバン大学医学教育プロジェクト

欠田　早苗　　(兵庫医大・二解剖)
岩崎　忠昭　　(兵庫医大・一内科)

1980年に援助計画について両国の代表者の間で署名をかわした。その内容は専門家の派遣，機材の供与，研修員の受入れを有機的に結びつけて，医療要員の要請，診療のレベルアップ，および医療教育水準の向上を図ろうとするものである。本件の実施要領は5カ年を第1期の教育病院建設前(1980—1982年)と第2期の教育病院建設後(1983—1984年)に二分した。

ここにいう専門家の派遣とは技術移転を目的として，労務提供ではないのである。機材供与は第1期を基礎部門，第2期を臨床部門を中心に供与することとする。1980年度は3千万円とし，ネパール側の原案に沿って行う。5年間に総額は3億円とする。研修員受入れは総枠を30名とし，受入れ機関は兵庫医科大学を中心とすることに決定した。以上は技術協力である。その後，1982年に教育病院第1期工事分（外来棟，検査管理棟）の完成（1978年設定，12.5億円）同2期工事分（手術棟，病棟）の完成（1979年設定，18.5億円）後の検討，調整の打ち合わせ団が派遣された。病院建設は無償資金協力である。

援助協力の実施についての問題点は，専門家派遣については，ネパール側から正式要請が提出されなかったことと，長期の労務提供型のものに傾くことである。研修員の受入れについては総計30名の受入れは日本側としては不可能であること，臨床分野において，日本では医療行為を行うことが，制度上不可能なことである。この点について，病院と期間を限定した一時的な医師免許証の発行と，リサーチ活動への参加の要望があった。看護分野では日本語の習得の困難さが特にあげられ，ことに医学用日本語の理解に時間がかかる。機材供与については新しく完成する病院の運営に当たって，無償資金協力に含まれる機材供与も活用することになった。

病院は1985年3月に完成し，ネパール側に管理は移された。5年にわたる技術援助は終了したが，両国の関係者が協議した結果，さらに3年の延長が合意され，将来にむけて問題となることは，機材については輸送時間と故障の問題，さらに教育機材の送付も望ましい。また，消耗品を含めてネパールの技術水準を考慮する必要がある。日本から帰国した研修員の技術指導のための専門家派遣を活発化する必要がある。また，双方の間で問題にされなかったが，今後，ネパールの国情にあったcommunity physicianの養成を通じて，保健水準の向上を進める。さらに，この援助を予定計画した時点からは5年を経過し，その間に医療技術が進歩し，この進歩に見合った新しい援助が必要となることである。その他病院開設と同時に問題とされたことは，医療従事者の清潔感覚，勤務時間や病院の管理経営方式についての助言の必要なことである。

5h フィリピン共和国熱帯医学研究所プロジェクトからみた医学医療協力

布上　薫　　(九州大・医技短大)

フィリピン熱帯病感染症による高罹患率，高死亡率が国民衛生に重大な問題である。過去にマラリア，住血吸虫症，結核，およびコレラの研究プロジェクトがそれぞれ個別に実行され，日本人もこれらに参加協力してきた。同国の医療関係者は，米国のNIHのような研究機関を持つことに夢がある。1981年4月熱帯医学研究所（RITM）が開所され，小さいが熱帯病感染症の総合研究所として1982年より実動を開始した。私は初の臨床ウイルス学の専門家として1981年9月から6カ月間滞在し，本年8月に5年間の評価に参加，その発展をみることができた。RITMはJICAを通して日本が建物と設備機器を提供し，フィリピン政府の財政的支持によって運営されている。国際的にもWHO，カナダ，オーストラリア，米国などから研究費の支援をうけられるように評価されてきた。研究の課題は，呼吸器感染，下痢症，住血吸虫症，

髄膜炎，肝炎，マラリア，癩，フィラリア症など重点的にしぼられた。病原解析により，肺炎・下痢・髄膜炎の起炎菌の頻度を明確にしてきた。この仕事の中で下痢症におけるロタウイルスの病原性の重要性を確認した。大腸菌ではその毒素産生性による分類も行う。多くのウイルスが分離同定された。インフルエンザA，B，パラインフルエンザ1－3，RSV，アデノ，ポリオその他のエンテロウイルス，麻疹，ムンプス，単純ヘルプス，デングなどである。フィリピンでは知識としてよく知られながら，初の分離ウイルスも多い。国内でこれまで未経験のデータが，自らの手で出来上がることは，同国の研究者に強烈な感銘を与えた。これらのデータは合理的な予防医学対策の基礎となる。RITM の臨床部門は約80%が小児で，90%以上が感染症であり，地域医療の奉仕とともに研究上にも貢献している。研究部門と臨床部門を通じて，レジデントとフェローがフィリピン大学病院を含めた関連病院から，感染症の卒後修練に参加し，希望者が増加している。地域の公衆衛生活動のための，医師の研修も行う。医療・検査技師の研修コースも設けている。このように次代を担う医師をはじめ，医療関係者の熱帯病感染症の教育訓練に，大きな役割を演じるようになってきた。

日本は建物・設備機器・専門家を提供し，これまでに紹介した研究成績に，直接関与してきた。医学医療協力の成果は今後の自主運営と国民健康の改善による。専門家は日本の国内発想でなく，その国のニーズに合わせて経済的で生産的，実行可能な技術を考える必要がある。このような専門家の育成や，帰国後の評価，身分保障などは日本の国内的に不備な点が多く，個人の犠牲を強いていることがある。発展途上国への医学医療協力のためには，当局の国際，国内的視野をもった慎重な配慮が望まれる。

Ⅲ　熱帯地における旅行者感染症
—その現状と対策を中心に—

1　司会のことば

中林　敏夫　　(阪大・微研・原虫)
青木　隆一　　(大阪市立桃山病院)

わが国と諸外国との交流促進に伴い，年間450万人もの渡航者，200万人もの来日者が数えられる。特に熱帯地開発途上国との国際間旅行者数は，増加の一途をたどっている。加えて航空機輸送の発展により，諸外国との時間的距離が著しく短縮した。過去十数年来，コレラ，マラリア等の輸入感染症問題が注目され，また1969年のナイジェリアにおけるラッサ熱の発生を契機に国際伝染病対策の急務が叫ばれるに至った。

本シンポジウムでは単に輸入感染症問題としてでなく，熱帯地旅行者にとり特に重視すべき諸感染症をテーマとして，各分野の専門家に，発生の現状と対策問題を中心として，解説願うこととした。

青木博士は，過去3年間の帰国者感染症患者所見を中心に，最近の疾病の傾向とその見解を述べられる。若年者の罹患が多く，腸管感染症に加え，不明熱，肝疾患等が注目される。

今川博士は，いわゆる国際伝染病であるラッサ熱，マールブルク熱，エボラ出血熱について解説される。現地の無対策現状の故に，旅行者は野鼠との接触を避けねばならない。ワクチン開発の現状や，Ribavirin の治療効果に触れられる。日本における高度安全病棟が不可欠の対応となる。

志方博士は，熱帯地に多いウイルス性肝炎問題について，A型肝炎，B型肝炎の他に非A非B型肝炎を解説される。ヒマラヤに分布するものや，デルタ肝炎の特徴などにも言及される。肝炎問題は，熱帯地旅行者感染症として，ますます重要なものとなろう。

細菌性腸管感染症に関し，竹田博士はコレラ，および毒素原性大腸菌感染を中心に説明される。また，多剤耐性赤痢，腸炎ビブリオ感染についての諸問題や経口輸液について述べられる。

高田博士は，マラリア発生と対策問題を解説される。特に PHC に統合された新しい対策法の持

つ特徴や，その難点に触れられる。また新治療法や，ワクチン開発の現状を話される。

輸入熱帯病の薬剤治療法に関する研究班（厚生省）による，薬剤の供給と治験が進められてきた。尾辻博士は自験例を中心に治療法とその効果について解説され，主に，マラリア，アメーバ赤痢，糞線虫症などの熱帯寄生虫問題を詳述される。

各演者の発表は短時間で，十分に意を尽くした報告とはなり難いが，広範囲に及ぶ熱帯地旅行者感染症の重要性と，それぞれの項目について最新の知見が述べられるものと期待している。

2　帰国者における感染症の現状

青木　隆一
（大阪市立桃山病院・感染症センター）

現今の国際化時代を反映して，わが国でも欧米の発展国と同様に，発展途上国よりの「輸入感染症 (imported diseases)」が急激に増加し，防疫や診断・治療面での新しい対応が重要視されている。大型高速のジェット機による大量輸送時代に入って海外旅行者が急増し，特にインド亜大陸やアフリカ大陸の奥地に気軽に出掛け，短時間の間に帰国しうるようになって，現地で罹患しても潜伏期の間に帰宅して家庭や職場に二次感染を起こしたり，長期間の treking で無症状保菌者として帰国し，感染源となるケースも増え，「国際化時代の落し子」として旅行者感染症，輸入感染症対策が強く要請されている。

1974年より1985年10月末までに大阪市立桃山病院に入院し，病原微生物が明らかになって確認しえた感染症患者は，総計383人に達し，複数微生物感染は41件である。この期間を4年毎に3期に分けると，第1期は海外駐在員か長期出張者の持ち帰る深刻な暗い時期で，腸チフス・パラチフスAなどが多かった。第2期（1978—1981）は，東アジアか東南アジアに集団で慰安旅行に大量出掛けるセットツアー時代で，細菌性赤痢が急増し，また腸炎ビブリオ，サルモネラのような古典的食中毒の多い時期であった。第3期（1982—1985）は若い世代，20歳台の大学生やＯＬたちが大量インド亜大陸（インド，ネパール，パキスタンなど）に，長期間の徒歩旅行を楽しむ時代（トレッキング時代）に入って，imported disease，旅行者感染症も急激に変貌し，細菌性赤痢に加え，新認定の食中毒菌，Aeromonas, Campylobacter, NAG-Vibrio, Plesiomonas などの「複数菌感染」が主体を形成し，他方，マラリアやウイルス肝炎なども相対的に増えて来た。また海外旅行者感染症の入院は，正月明けと夏休みに多かったが，最近では若い大学生やＯＬの春休み明け，5月の連休明けにも増え，新しい入院のピークをみるようになった。

旅行先，推定罹患地域も東アジアや東南アジアの近隣国から遠くインド亜大陸やアフリカ大陸，オセアニアや中南米に拡大され，特にインド亜大陸が急増し，旅行期間も1—2カ月の長期のトレッキングが主流となった結果，わが国の旅行者帰国時感染症，imported disease も大きく変貌をとげ，英国型のそれに類似するようになって来た。このため，英国と同様，医療人の再教育や一般の海外旅行者の啓発，帰国時の健康診断の必要性が高まり，新しい対応が強く要請されるに至った。

3　国際伝染病—ラッサ熱，マールブルグ病，エボラ出血熱—について

今川　八束（都立墨東病院・感染症科）

国際伝染病とは，わが国で患者の取扱い上行政的に用いられる用語であり，ラッサ熱 (LF)，マールブルグ病 (MD)，およびエボラ出血熱 (EHF) をいい，LF は指定伝染病となっている。

発生状況：LF は1969年ナイジェリアで確認されて以来今日まで，10名以上の院内感染6件を含む21件392名（死亡102名）の記録があり，ギニアから中央アフリカに至る西アフリカに，MD は1967年ウガンダから輸入されたアフリカミドリザルによる感染が西独，およびユーゴスラビアで発生して以来，南ア，ケニア，ジンバブエ等の東，南アフリカで4件37名（死亡9名）が，EHF は1976年スーダンとザイールでの大流行を含め6件651名（死亡458名）が，ケニアを含めて報告されている。

アフリカ以外では，LF は英国で10件10名（死亡2名），米国で3件3名（うち実験室感染2名1名死亡），と西独，オランダ，オーストラリア

で各1名の輸入例があったが，輸送中を含めて二次感染症はなく，MDは前記西独，およびユーゴの二次感染症を含め31名（死亡7名）の他にはなく，EHFは英国で1名の実験感染症が記録されている。

ウイルス保有動物および伝播様式：ラッサウイルスはアフリカのサバンナに広く生息する*Mastomys natalensis*が保有し，尿および唾液から排泄される。MDとEHFウイルスは齧歯類の保有が疑われているもののなお不明である。ヒトへは注射器事故のような皮膚創傷を介しての感染が主であるが，重傷患者との濃厚接触によるエアロゾル感染も存在する。

臨床症状および鑑別診断：ウイルス性出血熱の範ちゅうに入るが，発病はインフルエンザ様の非特異症状で始まり，臨床診断の決め手はない。最も鑑別を要する疾患とマラリアと腸チフスである。

ウイルス学的診断：患者から長期間ウイルスが分離されること即ち血液（LF 19，MD 15，EHF 8病日），咽頭（LF 19，MD 6病日），尿（LF 32，MD 7病日），精液（MD 83，EHF 61病日），および潜伏期間の長いこと（最長LFの17病日）は，患者や接触者の取扱上問題となっている。

予防並びに治療：現在特殊療法として，それぞれの回復期患者のプラスマの早期投与のみが有効である。しかし1977年モザンビークで*M. natalensis*から分離されたアレナウイルスは，ラッサウイルスと免疫学的に強い交差反応を示し，サルのLF感染防止に有効であった。又抗ウイルス剤Ribavirinもサル LFの治療に有効であったとの報告もあり，ともに今後の進展が期待される。

旅行者の注意：英国では1982年44名がアフリカからの帰国後，ラッサ熱等を疑われて入院したが，うち26名はナイジェリアからで，うち2名がLFと診定された。経験上地方の病院勤務者，調査あるいはプロジェクトで働いている者に危険性が高いという。

わが国の対策：患者の収容はベッドアイソレーター，およびP4臨床検査室を備えた都立荏原病院の高度安全病棟に，ウイルス学的検査室は予研村山庁舎に，患者輸送用アイソレーターは，成田，大阪空港，および東京都に各1台用意されている。

4　ウイルス性肝炎について

志方　俊夫　　（日本大・医・病理）

熱帯地方においてウイルス性肝炎は，日本人の旅行者あるいは在留邦人にとって腸管感染症についで多発する疾患であり，無視できない重要な病気である。B型肝炎とは潜伏期が長いので，これらの地方への旅行と直接の関係を証明するのが困難なことがある。

ウイルス性肝炎は感染症の中でその解決がもっとも遅れたものの一つであるが，これはその起因ウイルスが，長い間見つからなかったためである。しかしBlunbergのオーストラリア抗原の発見を契機にして，まずB型肝炎ウイルスが見つかり，ついでA型肝炎ウイルスも見つかった。しかしA型とB型肝炎の確定診断が出来るようになると，A型でもB型でもない肝炎の存在がはっきりしてきたのである。これを現在仮に非A非B型肝炎と呼んでいるが，この中には日本など先進国で輸血などに関連して見られる非A非B型肝炎と，インド，ビルマなどヒマラヤ山麓の国々で見られ，経口感染で伝播する非A非B型肝炎とがある。またB型肝炎ウイルスをヘルパーウイルスとして感染する，デルタウイルスも問題になる。ここでは個々のウイルスの感染経路，予防法などを簡単に述べた。

A型肝炎は日本国内では戦後急速に減少し，日本人の35歳以下の人は，5％位しか抗体を持っていない。熱帯地域では今なお常在しているが，A型肝炎に対して抗体のない日本の若い人がこれらの地域に行くと，またたく間にA型肝炎に感染する。A型肝炎は子供が感染した場合は軽くかかるが，成人が感染すると重くなるという事もある。予防にはγグロブリンを接種して行けばよいが，ワクチンはまだ出来ていない。

B型肝炎は日本国内でもまだあるが，東南アジア，アフリカではHBVのキャリヤー率が高く，日本にいるより感染する機会は多い。感染は医療機関で起こる事もあるが，性行為により主として感染する。成人が感染した場合急性肝炎ですむが，家族を伴って海外に赴任し子供が感染した場合，将来肝硬変，肝癌になる事がある。ワクチンは既

に出来ているが，ワクチンの接種に6カ月かかる事を考えておかなければならない。

デルタウイルスは，B型肝炎ウイルスをヘルパーウイルスとして同時に感染する。ただデルタウイルスの混合感染があると症状が重くなり，しばしば激症肝炎で死亡するから注意をしなければいけない。

主として輸血で感染する非A非B型肝炎は，むしろ日本国内で感染する事のほうが多いかもしれないが，熱帯地域でも医療機関で感染する機会はある。

経口的に伝播する非A非B型肝炎は，インド，ビルマを始めヒマラヤの山麓の地域にみられる。経口的に感染し，しばしば流行する。妊婦あるいはB型肝炎ウイルスのキャリヤーが感染すると症状が重くなり，死亡率が高い。

5　細菌性腸管感染症

竹田　美文（東大・医科研・細菌感染）

熱帯や亜熱帯地方への旅行者が，旅行中に下痢を訴えることはかなり古くから知られている。たとえば，Montezuma's revenge という言葉は，旅行者下痢症を意味するが，これはメキシコのAztec 族最後の皇帝であった Montezuma II 世(1503—1520) を攻めた軍隊が，下痢が原因で戦意を失い敗退したところから，下痢のことを皇帝の復しゅう (revenge) であると恐れたことに由来しているといわれる。

大阪空港検疫所における旅行者下痢症の原因菌検索成績によると，わが国の海外旅行者の旅行者下痢症のうち，もっとも多いのは毒素原性大腸菌感染症で，次いでサルモネラ症，腸炎ビブリオ感染症が多い。この3つが，原因の確定した細菌性腸管感染症の約90%を占める。赤痢やコレラは，前3者に比べると患者数は少ない。しかし熱帯地においては，細菌性腸管感染症としては，前3者よりも重要である。わが国においても，法定伝染病であるところから，より慎重な取り扱いが要求されている。

1961年よりはじまった現在のコレラの第7次世界大流行は，ますます拡大する傾向が強く，終息する気配がない。流行の主要菌型はエルトール型菌であるが，1982年秋からバングラデシュにおいて古典型菌の流行が繰り返されている。古典型菌によるコレラは，一般的にいって，エルトール型菌によるコレラよりも重症の場合が多く，治療を施さなかった場合の致命率も，前者の方がはるかに高い。わが国では，1977年の有田市における流行以来，毎年数十名のエルトール型菌によるコレラが報告されている。その殆どが海外旅行者である。

毒素原性大腸菌が旅行者下痢症の原因菌として極めて重要であることは，1975年頃から広く認められるようになった。わが国の旅行者下痢症においても，その約20～25%が毒素原性大腸菌によることがわかっている。国内でも集団食中毒事例や散発事例の発生が相ついで報告されているが，これらが国外から持ち込んだ菌による可能性が少なくない。早急な対策が必要である。

コレラや毒素原性大腸菌感染症の場合に見られる水様性下痢の治療に，WHO の推奨する経口輸液 (Oral Rehydration Solution, ORS) が開発途上国では広く使用されていて，めざましい治療効果を挙げている。組成は1リットル当たり，食塩 3.5g, 重炭酸ソーダ 2.5g, 塩化カリウム 1.5g, グルコース 20.0g から成っている。原因菌の除去には役立たないが，対症治療剤として，旅行者が簡単に使用できる利点がある。わが国においても，旅行者下痢症のみでなく，一般の臨床でも広く利用することを検討すべきであろう。

6　マラリアについて

高田　季久　（大阪市大・医・医動物）

WHO の指導による MEP (Malaria Eradication Programme) は当初は素晴らしい成果を収め，20カ国以上でマラリアが根絶された。しかし1960年代末から1970年代にかけて，熱帯各地で激しい再燃が起こり，場所によっては MEP 開始以前とあまり変わらない程の流行がみられる場所さえ出て来た。

1985年の WHO の報告によると，1983年の世界の総人口46億7600万人のうち，マラリア汚染地区に住居する人々は，約半数以上の26億1600万人である。そして毎年2億人以上のマラリア患者と

200万人以上の死者があるものと推定されている。

この再燃の原因については，経済的な破綻，媒介蚊の殺虫剤抵抗性，原虫の薬剤耐性など，多くの要因が関与しているが，いずれにしても汚染地区ではマラリアによる生産性の低下が貧困を増大し，非汚染地区では旅行者による輸入マラリア症例と死亡例の増加が大きな問題となっている。

この様な再燃に対して WHO は1970年代中頃に MEP から MCP (Malaria Control Programme) への作戦変更を行うと共に，1970年代末に MCP を4種の戦術様式に区分し，当面各地の実情に応じた実行可能な方法で実施することとし，さらに MCP を各国の PHC (Primary Health Care) 組織に統合して実施するように勧告した。そして熱帯地への旅行者の安全のための指針として，毎年世界各地のマラリアの現状と予防法をまとめた "Malaria Risk in International Travel" を公表している。

一方実施面では，かつて成虫蚊対策と患者の発見治療を主体とした対策に改善が加えられ，幼虫対策をも含む各地区に適した方法を採用することとし，同時に新しい殺虫剤や抗マラリア剤の開発など，MCP に関する各種の基礎的，応用的研究が世界的規模で推進された。

その結果1980年代には，アフリカを除く世界のマラリアは，1970年代に比して徐々に低下する傾向を示している。各種の基礎的研究の中でも Biotechnology を応用したマラリアワクチンの研究の進歩は特筆すべきものではあるが，残念ながら未だ応用の域には達していない。

最近マラリアの予防に関して大きな問題となっているのは，従来 Chloroquine 耐性熱帯熱マラリア汚染地区で広く用いられていた，Fansidar＋Chloroquine 併用予防内服を行った米人旅行者の中に激しい皮膚壊死，発赤，Stevens-Johnson 症候を示すものが多発し，6名が死亡したことが米国 CDC により明らかにされたことで，WHO もこの点を重視し，Fansidar などの合剤の予防内服は慎重に行うように勧告している (Wkly. Epidem. Rec., 60, 181–188, 1985; MMWR., 34, 185–194, 1985)。

わが国では幸いにまだこの様な報告はないが，かなりの旅行者が Fansider，又は類似合剤を予防内服しているものと思われるので，今後 WHO，CDC などの勧告を参考として，日本人に適した予防対策の立案，旅行者の追跡調査，輸入マラリア症例の確実な捕捉などのための組織作りが必要と考えられる。

7　治療薬剤からみた熱帯性寄生虫病

尾辻　義人　(鹿児島大・医・二内科)

海外との交流が盛んになるにつれて，輸入熱帯病の問題はますます重要性を増している。

わが国においては，現在寄生虫病薬は需要の減少と副作用という問題で，入手困難な状況が続いている。

このような寄生虫病薬の入手困難を解消する目的で，1980年度に輸入熱帯病の薬物治療法に関する研究班が結成され，輸入寄生虫病に対する治療薬剤の入手，保管，配布および治療効果，副作用などの検討を続けている。最近までの成績をまとめて報告する。

1980年度より1985年6月までに治療薬剤を配布した件数は506件で，都，府，県別にみると，東京都105件，鹿児島県101件，福岡県67件，大阪府45件と多く，おおむね全国各地に配布している。

さらに，疾患別では，マラリアが144件，糞線虫症119件，鞭虫症40件，旋毛虫症35件，肝吸虫症35件，カリニ肺炎19件，広節裂頭条虫症19件，アメーバ赤痢16件，ランブル鞭毛虫症15件などが多かった。

治療薬剤では，サイアベンダゾールに次いで，マラリア治療薬のプリマキン，クロロキン，ファンシダールが多く，その他メベンダゾール，プラジンカンテル，キナクリンなどの要望が多かった。

治療薬剤の医療機関別では大学が191件，国公立病院164件，私立病院52件であった。

次に輸入寄生虫は176件で，マラリアが133件と最も多く，日本人が103件，外国人が30件であった。また鞭虫症13件，肝吸虫症11件，ランブル鞭毛虫症9件でその他トリパノソーマ症，日本住血吸虫症，ビルハルツ住血吸虫症，旋毛虫症，無鉤条虫症などであった。

次にマラリア患者について検討した。マラリア

患者133件中，年齢別では30歳代55件，20歳代46件で，若者が大部分であった。マラリアの種別では三日熱マラリア67件，熱帯熱マラリア32件，四日熱マラリア１件，種別不明３件であった。感染地は日本人ではアジア地区45件，アフリカ地区42件，ニューギニアを含むオセアニア地区14件，不詳２件，外国人ではアジア地区22件と最も多く，次いでアフリカ地区４件であった。マラリア患者の業務内容では日本人は観光23件，学術調査15件のほか海外での業務の関係が目だった。外国人ではベトナム難民７件が目だっていた。

以上より，輸入熱帯性寄生虫病問題と治療薬剤の入手を容易にすることは，緊急な問題である事を痛感した。

Japan. J. Trop. Med. Hyg., Vol. 14 No. 2, 1986, pp. 115–150

PROCEEDINGS OF XXVII ANNUAL MEETING OF JAPANESE SOCIETY OF TROPICAL MEDICINE (1)

30 October–1 November 1985 Kobe

CONTENTS

5f Cooperative study by Indonesian and Japanese doctors on dengue haemorrhagic fever (DHF) Y. Funahara

5g The Tribhuvan University medical education project in Nepal S. Kanda and T. Iwasaki

5h Japanese cooperation for medical education through the Research Institute for Tropical Medicine in the Philippines T. Nunoue

Symposium: Infectious diseases of international travelers in the tropics -present status of epidemiology and control

Chaired by T. Nakabayashi and T. Aoki

1 Introductory remarks T. Nakabayashi and T. Aoki

2 The current states of imported disease at the Infectious Disease Center, Osaka Momoyama Hospital T. Aoki

3 International infectious disease—lassa fever, marburg disease, ebora haemorrhagic fever Y. Imagawa

4 Viral hepatitis in tropical areas T. Shikata

5 Bacterial enteric infections Y. Takeda

6 On malaria S. Takada

7 Present state of tropical parasitic diseases in view of therapeutic drugs Y. Otsuji

General presentation (will be appeared in the next issue)

Student presentation (will be appeared in the forth issue of Vol. 14)

Social meeting (will be appeared in the forth issue of Vol. 14)

Special lecture

DENGUE HEMORRHAGIC FEVER: A CRITICAL APPRAISAL OF CURRENT HYPOTHESES

LEON ROSEN

Director, Arbovirus Program, Pacific Biochemical Research Center,
University of Hawaii at Manoa, Honolulu, Hawaii

The clinical manifestations encompassed by the term "dengue hemorrhagic fever" are responsible for most of the hospitalizations and deaths among persons infected with dengue viruses. Since there is wide variation in the incidence of these forms of the disease from one dengue outbreak or endemic area to another, it is possible that a better understanding of their pathogenesis could lead to strategies that might prevent severe disease and death from dengue, even if the infection itself could not be prevented.

I should like to begin my presentation by commenting on the question. "Exactly what is dengue hemorrhagic fever and how does it differ from ordinary dengue fever?" In general, the more severe forms of dengue infection are characterized by hemorrhage, by hypovolemic shock, or both. However, there is a difference of opinion as to whether it is appropriate or useful to characterize all dengue infections with hemorrhagic manifestations as "dengue hemorrhagic fever". For example, the latest guidelines on dengue available from the World Health Organization (WHO) distinguish between "dengue hemorrhagic fever" on the one hand and "dengue fever with hemorrhagic manifestations" on the other. According to the WHO, the former is characterized by thrombocytopenia and hemoconcentration and can be divided into 4 grades. The hemorrhagic aspect of the first of these grades is limited to a positive tourniquet test. Thus, according to the WHO, a patient with a positive tourniquet test, thrombocytopenia, and hemoconcentration would be considered to have "dengue hemorrhagic fever", whereas a patient with severe, or even fatal, gastrointestinal hemorrhage and thrombocytopenia, but not hemoconcentration, would have only "dengue fever with hemorrhagic manifestations". Since thrompocytopenia is a common manifestation of all types of dengue infection and since children with fever, vomiting, or diarrhea from any cause can also have hemoconcentration, one can imagine the difficulty that at least some observers have in distinguishing the supposed difference between "dengue hemorrhagic fever" and "dengue fever with hemorrhage". As far as I am aware, there are no data, published or unpublished, which justify the distinction made by the WHO on either pathogenetic or prognostic grounds.

Fortunately for the purposes of this discussion, everyone agrees that there is an entity called the "dengue shock syndrome", which is one of the common forms, of life-threatening dengue, and which is usually, but not always, accompanied by hemorrhagic manifestations. In the interest of time, I will address the bulk of my remarks concerning pathogenesis to the dengue shock syndrome, but, in doing so, I do not mean to imply that the pathogenesis of the shock syndrome is necessarily the same as that of the hemorrhagic manifestations of dengue. The latter are so common in both mild and severe dengue infections and, as noted above, their

definition so controversial, that it is difficult to analyze any of the data with respect to their pathogenesis.

When the term "dengue hemorrhagic fever" came into use following the epidemics in the Philippine Islands in the early 1950's, it was at first believed, at least by some, that the severe forms of dengue represented a new clinical entity which had not been observed previously. I believe that it is fair to state that, at present, few persons, if any, hold this view. It is clear that the severe forms of dengue are now more prevalent than they were in the past. Unfortunately, there are no data to indicate whether this is the result, on one hand, simply of a quantitative increase in the incidence of all dengue infections, or, on the other hand, if the increase in severe clinical manifestations is the result of some qualitative change.

The outcome of any infection depends on the interaction between the infectious agent on one hand and host defenses on the other. In the case of dengue, there is a considerable difference of opinion as to whether it is the virus or the host that plays the predominant role in the pathogenesis of severe dengue disease. More specifically, there is a difference of opinion as to whether or not an acquired characteristic of the host, namely, a prior dengue infection with a heterologous dengue serotype consitutes, a risk factor for the development of severe dengue disease.

In this review, I should like to start with a discussion of the virus and then proceed to a discussion of the host. To begin with, one of the strongest arguments for an important role of viral virulence in the pathogenesis of severe dengue is that variation in the virulence of strains has been described for most, if not all, viruses for which appropriate assay systems are available. It would be surprising indeed if dengue strains and serotypes were an exception.

Epidemiologic evidence suggestive of differences in overall virulence between dengue serotypes is the observation that dengue types 2 and 3 have been more commonly associated with the dengue shock syndrome in Southeast Asia over the last 20 years than have dengue types 1 and 4. Since laboratory methods in use during that time period were least sensitive to dengue type 3, the association of that serotype with severe disease is especially convincing. Evidence for variation in virulence among dengue strains of the same serotype is more difficult to come by. For example, there have been many instances of relatively avirulent epidemics caused by dengue types 2 and 3, but alternative explanations, which I will discuss later, cannot be excluded. Unfortunately, dengue strains potentially different in virulence have not yet been analyzed by appropriate molecular methods. While oligonucleotide fingerprinting has been used to separate dengue strains of the same serotype into topotypes, the method analyzes only about 15% of the virus genome. Consequently, it cannot be expected to detect small differences of the type which have been found between virulent and avirulent strains of other viruses (such as poliovirus). Another major handicap in studies of dengue viral virulence is the lack of a laboratory animal or an in vitro marker for virulence. At present, the only way to assay the virulence of dengue viruses is in man.

While the concept of differences in dengue viral virulence is almost certainly, true, at least to some extent, there are certain epidemiologic observations from the South Pacific which are difficult to explain, unless virulence is a rather labile characteristic. For example, when dengue type 2 swept through the South Pacific, beginning in 1971, it was almost certain that the same viral strain was carried from one island to another. Yet, the virus caused relatively severe disease on some islands such as Tahiti and Niue and very mild disease on others such as Samoa and Tonga. The same phenomenon was observed with dengue type 1 beginning in 1975.

However, in the type 1 epidemics, severe disease occurred in Tonga and Niue, and relatively mild disease on Tahiti and Samoa. I might add at this point that the differences between the islands could not be explained by differences in prior experience with other dengue serotypes. Anecdotal evidence that dengue strains might change in virulence relatively easily, perhaps on the basis of rapid human to human passage, is the observation that a higher proportion of severe disease is often seen in the second half of an epidemic as compared with the first half. This was noted, for example, in Niue Island epidemic of 1972, Cuban epidemic of 1981 and also was described in the large Greek epidemic of 1927–1928.

I should now like to turn to a consideration of host factors in the pathogenesis of severe dengue. To begin with, I should like to comment on what might be considered two innate characteristics of the host, namely, genetic background and age, and then discuss an acquired characteristic, prior dengue experience.

It has been well documented in both laboratory animal models and observations on man that genetic factors can modulate the immune response of a host and hence the outcome of an infection. It would be surprising if the same were not true for dengue infections. At present, however, for dengue, only anecdotal observations are available on this point. First, one type of anecdotal observation is that it is not uncommon to observe multiple cases of severe dengue in the same family during an outbreak—far more frequently than might be expected to occur by chance. For example, in the Niue Island outbreak of 1972, there were 3 fatal cases among children in a single family out of a total of 12 fatal cases in a population of about 5,000. Second, there have been several examples of differences in attack rates for severe dengue among different ethnic groups during the same epidemic—for example, among Chinese in Malaysia. In most such instances, other explanations, such as differences in exposure to vector mosquitoes cannot be excluded. However, environmental factors have not been cited as an explanation for the relative lack of severe disease among blacks during the recent Cuban outbreak. If it were true that a small proportion of a given population was particularly susceptible to the severe manifestations of dengue because of genetic factors, this might provide an explanation for the dramatic decrease in the incidence of such severe infections after the first few epidemic waves of dengue shock syndrome in certain areas—such as has been observed in Manila in the Philippine Islands. A similar explanation has been suggested for the dramatic decreases in the death rate for measles in island populations during succeeding epidemics.

It is well established that, in virgin soil epidemics of dengue in which persons of all ages are infected, the common clinical manifestations of dengue, such as fever, are more severe among older children and adults as compared with younger children. This is similar to the experience with certain other infectious diseases, such as rubella and poliomyelitis, in which clinical manifestations are more severe in infected adults as compared with infected children. No data are available on possible age differences in susceptibility to the dengue shock syndrome. In those epidemics in which a sufficiently large number of such cases have occurred, data are lacking on the number of individuals in the different age groups susceptible to infection with the responsible dengue serotype or serotypes. It is of interest in this regard to recall the history of poliomyelitis epidemics. Paralytic poliomyelitis was originally called *infantile* paralysis because in early epidemics only young children were paralyzed. As poliovirus infection was delayed until later in life with improved environmental sanitation, it became apparent that older children and adults were actually more susceptible to the paralytic consequences of a poliovirus infection than were young children. In the first epidemics, paralysis was limited to young children because they

were the only ones not already immune. I will have more to say on this point in discussing the next item on my agenda.

I should now like to discuss the controversial question of whether or not a prior heterologous dengue infection constitutes a risk factor for development of the dengue shock syndrome. Two types of data have been cited in support of this concept. One of the types is experimental. It is said that lower primates experimentally infected with dengue type 2 virus develop higher levels of viremia if they have actively or passively acquired heterologous dengue antibody than they do if they have no such antibody. The other type of data cited in support of what can be called the "sequential infection hypothesis" is epidemiologic. Several studies are said to show that the dengue shock syndrome occurs more frequently during a second dengue infection than it does during a first infection.

Some of you may have noted that I have not mentioned as a supporting argument the voluminous literature on antibody enhancement of the replication of dengue type 2 virus in cell cultures. I do not doubt that such enhancement occurs in cell cultures—just as it does with other flaviviruses and viruses of other taxonomic groups. However, unless antibody enhancement of dengue virus replication occurs in the intact host, the *in vitro* data are irrelevant. As you will see, it is my opinion that the evidence with respect to intact hosts is far from convincing.

The data on antibody enhancement of dengue virus replication in lower primates consist of 2 studies from same laboratory. In the first study, it was found that in monkeys infected with dengue type 2 virus after a previous dengue type 1, 3, or 4 infection, mean peak viremia was higher than that of monkeys with primary infection with the same virus. Mean peak viremia for secondary type 1, 3, and 4 infection either was the same or was lower than that for the corresponding primary infection.

I do not find the data on dengue type 2 viremia convincing for the following reasons. First, the magnitude of peak viremia in the monkeys, as measured in this study, was extremely variable. For example, while the mean peak viremia in secondary infections was said to be 13-fold higher than that in primary infections, the variation in peak viremia from one individual animal to another in both primary and secondary infections was a 1,000-fold or more. The second question that I have about this study concerns the way in which viral titers were determined. The viral assay system used, namely plaque assay in LLC-MK2 cells, is known to be relatively insensitive, but that in itself is not a problem in a comparative study of this type. What is a problem is that the sensitivity of the system is known to vary from one test to another. In my opinion, viremia levels can be legitimately compared in this system only if matched pairs of specimens from primary and secondary infections of the same serotype were assayed in parallel. As far as I can determine, this was not done. Moreover, the fact that viremia was found to be higher in secondary infections with dengue type 2, but not with dengue types 1, 3, or 4, calls for an especially rigorous look at the data. Antibody enhancement of virus replication in cell cultures is not limited to dengue type 2, nor is the dengue shock syndrome caused exclusively by this serotype. As a matter of fact, dengue type 3 has been the predominant virus responsible for the syndrome in several recent epidemics in Southeast Asia.

The second experimental study cited in support of antibody enhancement in the intact host consisted of comparing the viremias in 2 groups of 5 monkeys each. Immediately prior to being inoculated with dengue type 2 virus, one group of animals was infused intravenously with a human serum pool known to have an *in vitro* dengue virus replication enhancement titer of greater than 1 to 2,000,000. The other group of animals received human serum without dengue

antibody. Three- to 50-fold higher peak viremias were observed in the animals which had received antibody as compared with those which did not.

The problem that I have in accepting this experiment as evidence for antibody enhancement in the intact host is that I believe that it may represent just another *in vitro* experiment. Unfortunately, the sera tested for virus content were not assayed for *in vitro* antibody enhancement titer. Such tests were carried out on sera drawn from monkeys shortly after they had been infused. The enhancement titer in those animals which had received antibody was found to be about 1 to 1,000,000. Given this high titer, I think it quite likely that *in vitro* enhancing antibody was still present in the monkeys' sera at the time of their viremia a few days later. If this were the case, the same data might have been obtained had the antibody not been given to the monkeys at all, but rather, just added to their sera after the latter were withdrawn for virus assay! There is no question that dengue plaque counts in LLC-MK2 cells can be increased by small amounts of antibody. When utilizing such cells for plaque reduction neutralization tests, we often have observed a larger number of plaques in wells with serum dilutions beyond the neutralization endpoint than in control wells without antibody.

I am aware of 4 other studies, involving man or lower primates, in which flavivirus viremia was compared in individuals with and without prior flavivirus infection. In 2 of the studies, the second infecting virus was a vaccine strain of dengue type 2. In one, vaccine was given to men who previously either had been vaccinated with yellow fever virus, or had not. In the other, vaccine was given to monkeys which had previously been infected with dengue types 1, 3, or 4, or had not been infected with any of the viruses. In the other 2 of the 4 studies, the second infecting virus was yellow fever. In one, yellow fever vaccine virus was given to individuals who previously had been infected naturally with Japanese encephalitis virus, or had not. In the other, virulent yellow fever virus was given to monkeys which previously had been infected with dengue type 2 virus, or had not. In none of these studies was a higher viremia ovserved in previously infected individuals as compared with those previously nonimmune.

In addition to this negative experimental data, in the course of extensive investigations of dengue epidemics of all 4 serotypes in the South Pacific, our laboratory has never observed that secondary infections were characterized by viremias that were, on the average, higher than those in primary infections, nor am I aware that anyone else has data to that effect.

It is, of course, impossible to prove a negative proposition. Thus, it is not possible to prove that antibody enhancement of dengue infection does not occur in the intact host. It can always be argued that such enhancement occurs only with certain dengue serotypes or strains, or only under certain special conditions. However, in view of the alternative interpretations which I have suggested for the 2 studies which are cited in support of the antibody enhancement concept. I believe that the burden of proof should still lie with those who believe it to be true. Confirmation of the experimental data by another laboratory, with modifications to meet the criticisms expressed, would be especially convincing.

The most impressive type of evidence for the sequential infection hypothesis would be epidemiologic. Several epidemiologic studies, all from Thailand, are said to be compatible with the hypothesis or to have demonstrated that certain sequences of dengue infection do increase the risk of the shock syndrome. I do not find these studies convincing because their conclusions are based on certain explicit or implied assumptions which either are not supported by data or are actually contrary to available information. The time available here is not sufficient for a detailed discussion of all the points of contention, but the following are some of the main issues.

In order to demonstrate that persons who have had a prior heterologous dengue infection are at greater risk of developing the shock syndrome than those who have not had such an infection, it is necessary to be able to define the denominators, that is, the 2 populations at risk. There are several problems in the epidemiologic studies in this regard. For example, at present, there is no serologic procedure which can determine if persons who have had more than one previous dengue (or flavivirus) infection are susceptible to infection with a given dengue serotype. Similarly, in the absence of virus isolation, it is currently impossible to identify the infecting serotype in a secondary dengue infection. Also, dengue viruses are transmitted by a vector with a short flight range and the risk of infection tends to be focal in distribution. Unless substantiating evidence is available, it cannot be assumed that an entire population will be uniformly exposed to infection with each of the dengue serotypes present in a study area. Then, there is the important question of whether or not individuals of different ages are equally susceptible to the risk of developing the shock syndrome. It cannot be assumed that they are. In fact, from what is known of other infectious diseases, such an assumption is unlikely to be correct.

There are also problems in the epidemiologic studies with respect to the numerator in the risk assesment, namely, the identification of cases and their correct classification with respect to prior dengue experience. It is important that there be no bias in the chance of detecting the 2 types of cases (that is, primary or secondary). For example, in the absence studies of virus isolation, which was relatively uncommon in the studies under consideration, any primary infection that was fatal, or one with only a single serum specimen, or one with a second serum specimen collected 7 days or less after onset, would be excluded from the numerator—since there would be no evidence of current dengue infection. Secondary infections can often be identified under those conditions because of the more rapid appearance of high-titered antibody. Finally, there is the very important problem of the serologic criteria by which cases are classified as primary or secondary. It cannot be assumed that the serologic responses of shock syndrome patients with primary infections will be the same as patients with primary infections and milder clinical manifestations. As a matter of fact, there is indisputable evidence that at least some patients with primary dengue infections and severe disease have unusually high antibody responses (usually characteristic of secondary infections).

It is impossible to prove that immune enhancement of dengue does not occur—since it can always be postulated that such enhancement occurs only with certain dengue serotypes, or only with certain strains of those serotypes, or only at very critical intervals of time. A well-designed prospective epidemiologic study would resolve the question—if immune enhancement of dengue was demonstrated. However, the low and unpredictable incidence of the shock syndrome, even in highly endemic areas, poses formidable problems for the design of such a study. There may be a greater chance of obtaining unequivocally positive data from retrospective investigations in particularly favorable environments. In the meantime, each person with an interest in the subject can take a careful look at the data presently available—and then decide for himself if immune enhancement of dengue is myth or reality.

SCIENCE AND TECHNOLOGY AND INTERNATIONAL EXCHANGE

MICHIO OKAMOTO
Member, Council for Science and Technology

Since the Meiji Restoration Japan has introduced science and technology from advanced western countries and succeeded economically by exporting the technological products. As it is well known, we have now the friction of technology and trade with advanced countries. Therefore it is the time for us Japanese to make efforts to be trusted by other countries.

First of all, we should invite foreign people to Japan and make them see the Japanese living in Japan instead of the Japanese living or travelling in other countries. And that is the only way to be truly understood by foreigners.

Secondly, we Japanese should create our own science, especially placing emphasis on the basic science research, which shall be not only seeds of our future engineering but also contribution to the whole world.

On the other hand, the problem of the impact of science and technology to human being has become serious, as it is seen in air pollution or destruction of nature. In this respect, too, we feel we have much to do to solve the problem as Japanese who have built our culture by adopting western and eastern culture. And it becomes important to discover the true Japanese spirit, in which especially the westerners are much interested.

In this international community, these are the important tasks for us Japanese; inviting foreign people to Japan, placing emphasis on the basic science research and discovering true Japanese spirit. And each of us should bear in mind that Japan has become a very important country in the world and contribute to the international exchange by ourselves.

Symposium

Tropical medicine and molecular epidemiology

1 INTRODUCTORY REMARKS

AKIRA ISHII[1] AND KUMATO MIFUNE[2]

Department of Parasitology, Okayama University Medical School[1]
and Department of Microbiology, Oita Medical College[2]

Recent technological advances in the nucleic acid research have enabled us to do the epidemiological research at the molecular level. In this symposium, recent progress of molecular genetics and/or molecular epidemiology of helminths, protozoa, bacteria and virus will be presented and discussed on the importance of molecular epidemiology in further studies of tropical medicine.

2 ANALYSIS OF ANTIGEN GENES OF HELMINTHIC LARVAE

KAZUO SUGANE

Department of Parasitology, School of Medicine, Yokohama City University

Larval antigens of *Toxocara canis* and *Trichinella spiralis* are useful for immunodiagnosis of visceral larva migrans or trichinosis. However, the small amount of antigen that can be collected from large numbers of larvae presents a problem. Recombinant DNA technology would be useful for producing large amount of antigen. *T. spiralis* infective larvae were cultured in methionine-free Eagle's MEM containing ^{35}S-methionine and ES or somatic antigen was extracted from culture media or larvae. The antigen reacted with infected mouse serum formed antigen-antibody complexes. The complexes were then absorbed by *Staphylococcus aureus* Cowan 1 strain and antigenic polypeptides were demonstrated by the autoradiography of SDS–PAGE. Total RNA was extracted from larvae by centrifugation through a CsCl cushion. *In vitro* translation of mRNA was carried out and an antigenic polypeptide with molecular weight of 48,000 in translation products was demonstrated by the autoradiography of SDS–PAGE. Poly(A)-rich mRNA was separated from total RNA in an oligo(dT)-cellulose gel column and antigen-specific mRNA was concentrated by the sucrose gradient centrifugation. cDNA was synthesized *in vitro* for cloning of antigen genes using bacteria. First and second strand of cDNA were synthesized according to the method of Buell *et al.* (1978) and Gubler *et al.* (1983) respectively.

3 RECENT PROGRESS IN IDENTIFICATION OF AFRICAN TRYPANOSOMES

HIROYUKI HIRUMI, V. NANTULYA, B. KUKLA,
O. OLE MOI-YOI AND P. MAJIWA
International Laboratory for Research on Animal Diseases, Nairobi, Kenya

Human and animal African trypanosomiases are caused by a number of trypanosomes among which, *Trypanosoma brucei gambiense, T. b. rhodesiense, T. b. brucei, T. congolense* and *T. vivax* are considered to be major pathogens. They are extracellular protozoan blood parasites transmitted by tsetse flies. Lack of simple and yet reliable methods to identify these species has hampered epidemiological studies of African trypanosomiases. However, various methods of identifying these species have recently been developed. In addition to the parasitological methods already available, trypanosomes can now be identified by modern analytical techniques using species specific monoclonal antibodies, isoenzymes, DNA hybridization probes and molecular karyotypes. These techniques have become useful tools to identify trypanosome species of experimental materials in laboratories. Further simplifications of the techniques are presently underway so as to enable their field applications to the epidemiological investigations of the diseases.

4 MOLECULAR EPIDEMIOLOGY OF ENTEROTOXIGENIC *ESCHERICHIA COLI* AND *VIBRIO CHOLERAE*

TATSUO YAMAMOTO
Department of Bacteriology, School of Medicine, Juntendo University

Enterotoxigenic *Escherichia coli* and *Vibrio cholerae* are important causes of infantile diarrhea in developing countries. In order to investigate virulence factors of enterotoxigenic *E. coli* and *V. cholerae,* molecular genetic techniques have been introduced. As a result, important new findings are increasingly being accumulated.

1. Enterotoxigenic *E. coli* (ETEC)

(i) Major virulence factors: ETEC colonizes the intestinal epithelium with fimbrial adhesins, and produces enterotoxins which cause diarrhea. Enterotoxins are divided into three distinct groups-heat-labile toxin (LT) and heat-stable toxins I and II (ST I and ST II).

(ii) Plasmid and transposon: Enterotoxin production is coded for by a plasmid, named ENT. In many instances, fimbrial adhesins are specified by a plasmid as well. The ST I gene has been found to be on a transposon—this finding was the first example of bacterial pathogenic transposons.

(iii) Fimbrial adhesins: Molecular cloning analysis of fimbrial adhesins such as CFA/I of human isolates and K88, K99 or F41 of porcine isolates have been reported.

(iv) ST: Complete nucleotide sequences of the ST I and ST II genes have been reported.

The mature ST I peptide region was found to be located at the C terminal of the genes.

2. *E. coli* LT and cholera toxin (CT)

(i) Gene and gene product: LT has structual and functional features in common with CT. The homology reaches 78% at the nucleotide level and 79% at the amino acid level.

(ii) Evolution of the genes: *E. coli* and *V. cholerae* diverged at ~670 Myears ago, while the LT and CT genes diverged more recently (~130 Myears ago).

(iii) Multiple copies of the CT genes: The CT gene, which is located on the chromosome, is flanked by repeated DNA sequences (RS1). *recA*-dependent recombination between the RS1 sequences results in amplification of the toxin genes.

3. *V. cholerae* virulence factors other than CT

Hemagglutination factors and fimbriae are noted in terms of the relatedness to intestinal adherence, and hemolysin, suckling mouse test-positive factor, PF factor and Shiga-like toxin as toxins. An invertible DNA was found at the upstream region of the hemolysin operon.

4. *Epidemiology*

Using the LT, ST I, ST II or CT gene as a probe, DNA-diagnosis of ETEC, *V. cholerae* and their related bacteria has been carried out by groups of J. B. Kaper, J. G. Morris, W. K. Maas and S. L. Moseley in the United States, and P. Echeverria in Thailand.

5 ROTAVIRUS INFECTION IN KENYA AS ANALYZED BY GENOMIC RNA

YASUO CHIBA[1] AND CHIAKI MIYAZAKI[2]

Department of Pediatrics, Sapporo Medical College[1]
and Department of Pediatrics, Faculty of Medicine, Kyushu University[2]

Human rotaviruses (HRV) have been established as one of the most important agents causing acute gastroenteritis in infants and young children. In developing countries, epidemiological studies have demonstrated that the illness due to HRV infection constitutes a major problem for the childhood health in terms of both morbidity and mortality. Patients with HRV infection usually have strong diarrhea and vomiting which may result in severe dehydration. Therefore, therapy for this illness consists of rehydration and adjustment of electrolytes imbalance. Although oral rehydration therapy is introduced experimentally in many countries, development of HRV vaccine must be the most important subject for final control of this illness.

HRV have 11 segments of double-stranded RNA as genomes. The molecular weight ranges from apporximately 0.2×10^6 to 2×10^6 daltons. These genomic RNA fall into 4 size classes and they will be demonstrated by PAG electrophoresis. Even RNA preparations extracted from purified HRV in stool specimens can be employed for this analysis. Electropherotypes of genomic RNA may differ from strain to strain and the most striking difference will be observed between the so called "long type" and "short type". HRV strain, with long electropherotype have antigenicity of subgroup II and serotype 1, 3, or 4. On the other hand HRV with short type has antigenicity on only subgroup I and serotype 2. It has also been demonstrated that various degrees of difference in the electrophoretic morbility of each RNA segment can be employed for identification of a strain from another and, thus, for detailed epidemiological

study or HRV infection.

We employed the analysis of genomic RNA for studying HRV infection of young children in coastal areas and Nairobi of Kenya from 1982 to 1983. On the coast, patients with this illness were detected during all months studied, and the average incidence of the infection was 25% (range, 8–45%). Analysis by polyacrylamide gel electrophoresis of viral RNA segments have revealed the existence of various strains of rotavirus. Thus, 18 representative electorpherotypes, including 6 short strains, were detected in 30 rotavirus specimens obtained from Nairobi, whereas 16, including 3 short strains, were detected in 70 virus specimens from coastal areas. With the exception of one strain, there were no identical electropherotypes between the 2 groups of rotaviruses obtained from these different districts. A change in predominant electropherotypes was observed in Mombasa in early 1983, and subsequently, newly occurring strains were detected in a small town along the coast when an apparant increase in gastroenteritis was observed in the district. Neutralization of tissue culture grown rotaviruses by specific antiserum have revealed the existence of three kinds of sero-types, *i.e.*, 1, 2 and 3, in both areas.

Therefore, it is suggested that HRV with various electropherotypes of genomic RNA are circulating in an endemic manner in heavily populated urban areas. The epidemics of HRV in rural areas may be influenced by the occurrence of new HRV strains in neighbouring large cities. These results clearly indicated that analysis of genomic RNA is useful for an epidemiological study of HRV infection.

6 OLIGONUCLEOTIDE FINGERPRINT ANALYSIS OF STRAINS OF GETAH VIRUS AND JAPANESE ENCEPHALITIS VIRUS

HIROYUKI HORI, KOUICHI MORITA AND AKIRA IGARASHI
Department of Virology, Institute of Tropical Medicine, Nagasaki University

Strain differences among 19 isolates of Getah virus from Japan and Malaysia and 38 isolates of Japanese encephalitis virus from Japan and Southern Asia were examined by RNase–T1 resistant oligonucleotide fingerprint analysis on their genome RNAs. The fingerprint patterns of certain host-dependent temperature-sensitive (ts) mutants differed from that of the parental Getah virus strain. Also, there were some differences in large oligonucleotide spots between strain isolated in suckling mouse brain (SMB) and strain isolated in mosquito clone C6/36 cells, despite the fact that both strains were derived from the same wild mosquito homogenate. In addition, many host-dependent ts mutants were present in mosquito strain, whereas no such mutants were observed in SMB strain. It is concluded that there is considerable variation in the strains of Getah virus infecting mosquitoes in the wild, and also that the variants or mutants present in mosquitoes might be subject to selection during viral multiplication in the mammalian host. For both viruses, isolates in the same geographical area and in close chronological isolation histories showed similar fingerprint patterns which were different from those isolates in different geographical areas or chronologically different histories. The data suggest that mutations and selections of both virus genomes proceeded independently in geographically different areas.

Tropical countries and Japanese medicine

1 INTRODUCTORY REMARKS

KONOSUKE FUKAI
The Foundation of Research Institute for Microbial Diseases, Osaka University

Medical cooperation in not only important for the promotion of health status in developing countries but also really important to dissolve tension among countries towards the establishment of security of the world.

Points of discussion in the symposium would be: Is Japanese medical cooperation well responding to the request of recipient countries? How existing way of implementing cooperation are evaluated; what is the way to improve present status? What is the key point to assist promotion of health status in each country at national level? What is the main cause of frictions between recipient and donor sides? How Japan should contribute in WHO's HFA and EIP programs?..., etc..

Frank and constructive discussion, opinions and critics essential to create future progresses are welcome.

2 THE IDEAL WAY OF INTERNATIONAL MEDICAL COOPERATION

2a THE PROBLEMS IN THE INTERNATIONAL MEDICAL COOPERATION

SHIGEO HAYASHI
National Institute of Health, Japan

The medical cooperations are urgently needed in the developing countries where the majority of the people are still suffering from a variety of dreadful communicable diseases, malnutrition and eventually a high rate of mortality. Japan in now among the countries which are expected to and should extend the aid to relieve the sufferings. In fact a considerable number of activities have been carried out by the governmental and non-governmental organization or even by the individuals. However, the history of Japanese cooperation with developing countries is yet rather short and it seems necessary to accumulate much more experiences in order to cope with all kinds of troubles encountered and to achieve better cooperations. Exchanging of information and sharing of experiences among the persons who are keen in cooperation are to be of great value for the promotion of more effective cooperations.

The experience clearly indicates that the most effective cooperation is achieved by the transfer of technologies and the training of personels in order to develop the self-rilience. However, it is primarily necessary to identify the technologies suitable to the recipient counry and, then, to find the efficient ways of transfer. There are problems to be considered for the

proper selection of technologies as following;

1) The need awared and the priority given by the recipient country as to the technology to be transferred. 2) The ability of the recipient to successfully receive the technology concerned. 3) The existence of system and machinery which are capable to utilize the transferred technology.

In case when a technology is considered to benefit greatly a country, but the conditions are not recognized suitable for the transfer, it will be necessary to cooperate first in enhancement of ability to accept that technology. There are many ways for the improvement of the capability. The dispatch of experts from Japan combined with donation of required instruments and materials, and the training of competent personels either in recipient country or in Japan are very effective.

Further it must be stressed that in assessing the success of transfer of any technology the effect of the application of the technology concerned should be evaluated in advance in multiaspects. Not only the medical but also socio-economical, agricultural and many other expertises are to be taken into account. For example the construction of a dam would eliminate the rapids in the river, the breeding sites of onchocerciasis vector flies, but would possibly expand the breeding places of malaria vector mosquitoes by stagnating the watercourse. Careful assessment and selection of proper technology to be transferred are essential for the success in cooperation with developing countries.

2b PRESENT ACTIVITIES OF THE ICMR OF KOBE UNIVERSITY SCHOOL OF MEDICINE —ITS IDEA AND GOAL—

SEIZO IWAI

International Center for Medical Research, Kobe University School of Medicine

We have been carrying on the scientists exchange programs of medical field between ASEAN countries for almost 7 years. The purpose of this exchange is to help scholastic activity through collaborate research works, which has been selected as important subjects for the human health care in particular country. We have selected 10 subjects so far, and 133 scientists have accepted and total 255 senior scientists were sent with great satisfaction.

Promotion of scholarship for scientists can not be established in a decade. Understanding of living backgrounds, educational and research environments in each country is very important factor for the success of the exchange program. And establishment of national supporting system for this program is also necessary, otherwise it may create frustration among them and will fail to promote future development.

3 EVALUATION OF JAPANESE MEDICINE BY RECIPIENT COUNTRIES

3a IMPACT OF JAPANESE MEDICINE IN THE PHILIPPINES

E. O. DOMINGO
University of the Philippins

Introduction: The impact of Japanese medicine in the Philippines is too early to measure. This is not to say that Japanese scientists have not made significant contributions in medicine for indeed they have. But contribution to the pool of knowledge on a given medical problem does not necessarily produce an impact on the problem. In a country like the Philippines however effective solution rather than the totality of knowledge on a specific problem in more likely to produce impact.

My presentation today will deal on my personal perception on how Japanese medicine can produce an impact in medicine in the Philippines. I define impact here from the point of view of the subject population rather than from the perspective of the scientists.

Impact of American (Western) Medicine: Because of our historical heritage, we can say that Japanese medicine is relatively new to us, in point of time, not quite 3 decades old. Generous and substantial trial in medicine by Japan started only in the 70's, this is much too short to be of any consequence. For example, there is as yet no significant cadre of health workers in the Philippines whose training and orientation bear the Japanese imprint. In contrast, American influence is everywhere. Practically every health leader, teacher, researcher, practitioner and technician of consequence can claim some period of training and preparation under American tutelage. The impact of this influence is very palpable in the medical curriculum, postgraduate training, hospital system and yes, even research. It can also be claimed that American medicine has tremendous impact on eradication of some preventable diseases since it was the early American military doctors who instituted mass vaccination.

All these influences of America came about in a very specific set of circumstances which is probably best summed up in one work, colonization. At the present time colonization is hardly recommended. If Japan were to exert influence or attempts to provide direction in medicine in the region, it will do so under a different set of circumstances.

Inevitability of Japanese Influence: Given the current regional realities, it is inevitable that Japan should play a bigger role in health in this part of the world. Already acceptance of Japanese training in-lieur of Western training is becoming common place. It might in the very near future be the mode than the occasional exception. Japan can very well play the role, that is provide the leadership, in many aspects of health. This role is a consequence of and dictated by, the bountiful fruits of Japanese economy. A very brief review of the world and Asean scene in the general area of research and development (R & D) which includes the health field will illustrate my claim.

In the mid-70's the total world annual expenditures for R & D was about US $108 billion. Six countries (U. S., U. R., France, West Germany, Japan and the U. S. S. R.) accounted for 70% of R & D expenditures and 65% of world GNP. Japan alone accounted for 10% of R & D

expenditures. In relation to GNP, the same 6 developed countries spent about 2% to 4.6% of GNP on R & D.

Private sector resources for R & D has been very substantial in developed countries. In Japan, the private sector has provided as much as 70%. In the Philippines, about 90% has been provided by the government.

Basic research, in relative terms, has received a smaller but significant share of the R & D budget. In Japan, it is about 15.6% and in Mexico, about 19.2%. In developed countries, universities tend to do more basic research while private companies tend to do more development work.

Utilization of indigenous technology has been the pattern in developed countries. Nevertheless, there has been much technology transfer among advanced countries.

Even the most deliberate effort to do otherwise can not eliminate Japanese influence in the region by virtue of the vast resources of Japan that spills over in many endeavors including that concerning health. I have no doubt that our Japanese colleagues in the profession would like to have this influence create an impact.

Japanese and Philippine Orientation in Tropical Medicine: Japanese interest in tropical diseases is both historical and practical. Japan is located in a region surrounded by countries with these maladies. Its health workers therefore should retain the diagnostic and therapeutic acumen in dealing with these disorders because they can always be transported to the country due to massive movements of people both Japanese nationals and visitors. Japanese scientists are most likely attracted to these diseases only as models for investigation or in the pursuit on more basic researches like molecular biology, host-parasite relationship immunology and the like. On the other hand, to Philippine scientists concern for these diseases are brought about by necessity since these are daily facts of life with morbid effects, fatal consequences and significant economic repercussions. Philippine scientists where they request financial support from local sources will have to always answer the question of what is the impact of the research on the disease or problem. Invariably, impact here is meant to mean eradication, attenuation and/or control. However, if reseach has to be done to fill gaps in the knowledge to enable control measures to be developed, then the nature of the research may take many forms.

A requirement therefore, at least from the Philippines point of view on any activity in the health fields, more especially in tropical diseases, is its impact potential.

Impact Potentials of Japanese-Philippine Collaborative Research in Tropical Medicine: Involvement of Japanese scientists in research on tropical diseases in the Philippines is growing steadily. At the moment, the only research institute in tropical diseases in tropical diseases in the country was set up principally by Japanese aid thru JICA. The NAMRU, while also engaged in tropical disease research, is operationally under the full control of the United States government. There are many other collaborative medical activities between Japan and the Philippines under different sponsorship. The more noteworthy ones are those mediated by the JSPS and NSTA.

How are they faring? Have they created an impact? Yes and no. I will examine an example of that which has and has no impact. The purpose is to identify principles in the approach that caused one to have and the others to have no impact.

An example of a program that has all the potentials of creating an impact but did not is the program on schistosomiasis. Schistosomiasis is an important problem in the Philippines begging for solution. We know that with the available scientific knowledge control is possible if only

program research is emphasized over fundamental research. Let me elaborate on this. Japanese scientists I know have been working on schistosomiasis in the Philippines for sometime. However, their interest are centered on this parasitism. I am not saying that problems like pathogenesis of cerebral schistosomiasis or immunology of the disease are not important. They are. But they can be carried out as peripheral or corollary research within the context of a control program. It took Filipino scientists working with non-Japanese workers to undertake a project that is already creating an impact and at the same time, enables good research?

I will now recount the experience from a collaborative program in research in a tropical disease which in my opinion has created an impact within a short time. I refer to the collaborative research program undertaken by Japan and the Philippines through their respective national agencies namely the NSTA of the Philippines and JSPS. The essential chronologic activities of this program were:

1. Philippine and Japanese scientists after consultation identified a disease which is thought to be a major health problem by Philippine sciestists. This disease, hepatitis B, is *scientifically interesting* and at the same time *sufficiently important* to the Japanese.
2. The Philippine investigators aided by Japanese expertise and technology worked out the epidemiology, natural history and modes of transmission of HBV infection.
3. The Japanese scientists trained in their laboratories, Philippine scientists and technical personnel to enable them to perform serologic testing for HBV.
4. The Japanese then transfered the necessary technology to the Philippines to enable them to produce the materials to carry out continuing epidemiologic and diagnostic works.
5. The Japanese provided the Filipinos models a successful intervention scheme to control the disease and likewise helped them modify and simplify this to suit the Philippine situation.
6. The Japanese help the Philippines develop their own source of reagents for epidemiologic work and may be eventually for vaccine production.

The collaboration resulted within a 3-year period in;

1) Determination of prevalence and incidence of the disease
2) Establishment of transmission patterns and definition of population at risk
3) Development of control schemes
4) Enabling the Philippines to eventually be self-sufficient in reagents to continue surveillance work and assess success of intervention
5) Creation of awareness of the importance of the disease up to the level of policymakers

Feature of an Impact Producing Research Collaboration: From the two examples cited above, a few principles can be identified which increase the chances of creating an impact in tropical medicine collaborative research. These are:

1. Harmonizing the variant but not exclusivistic interest between the two sides brought about by differences in perspective orientation and objective. Research of "purely" scientific interest can ride with program research.
2. Level of collaboration and amount of work grow in an inverted pyramidal fashion.
3. Manpower development and technology transfer are essential parts of the collaboration.

Comment: Japanese influence in tropical medicine in the region is inevitable. To produce an impact certain principles must be observed.

3b MAN POWER DEVELOPMENT IN SOME UNIVERSITIES IN INDONESIA THROUGH COOPERATIVE RESEARCH PROGRAM WITH JAPAN

SUJUDI

Department of Microbiology, Faculty of Medicine,
University of Indonesia, Jakarta

Introduction: To develop some universities in Indonesia around the year 1952, affiliated programs were arranged between some universities in Indonesia and those in the U. S. A. All faculty members, junior lecturers as well as professors were sent to get the experience of how to run higher education in their field and to improve the skill in their field of science. The length of their education depended on what degree they were trained for the non degree program it lasted between 6 and 12 months, and for the degree program it lasted between 2 and 5 years. Several professors or senior staff from the U. S. A. were sent to Indonesia for 1 or 2 years mainly to develop a department and to complete a program of education which consisted of: setting up curriculum, giving lectures, guiding laboratory work and upgrading teaching staff. The affiliation was not simultaneously carried out in all universities in Indonesia. In some universities this began after the first phase program had been completed. The length of affiliation with one university could last for 10 years. The affiliation made some universities change their education system from Dutch system to more or less American system. Such a change happened especially in the system of Medical Faculty in which 7 years period of study became 6 years and the free study became guided study. The change did not make the quality lower but it increased the hospital training and produced more graduates. Apart from that, the affiliation made some universities become leading universities which guide, improve and help the development of the faculties of the newly founded universities in other provinces in Indonesia. The affiliation was made to improve the quality of undergraduate teaching and to increase the number of graduates.

Graduate program: In the later development it was felt that there was short age of scientists who had the ability to do research to analyze and solve problems in Indonesia. At that time the research staff were foreign scientists and Indonesians who studied abroad. To cope with those problems, around the year 1972 a plan to open educational program for graduate studies was started. The program for graduate studies was called strata 2 and strata 3, or Master and Doctorate program. The objective is to increase the number of scientists with more expertise in research and science. This program is not only performed in Indonesia but also by sending some teaching staff abroad. The first phase of this graduate program is to improve the ability of the teaching staff so that the quality of S_1 (under graduate) teaching could be raised.

JSPS program: In 1976 Kobe University Medical School offered a cooperative program which included joint research, exchange scientists and exchange information. University of Indonesia was very much interested in the offer so that after it had been studied, it was decided to accept the offer. Then it was submitted to the Directorate General of Higher Education (DGHE) to be listed as one of the cooperative programs between DGHE and Japan Society for the Promotion of Science (JSPS). There had been cooperative program previously between JSPS–DGHE in agriculture and optoelectronic/laser.

Joint research program: Joint research was conducted mainly in Indonesia between Japanese and Indonesian scientists. Both sides appointed their own coordinator respectively. The topics of the research were selected by both sides who considered them as problems. In the operation of the program Indonesia provided many young scientists who were later on expected to continue the research. Since it lasted between 1 and 2 months in Indonesia, it was necessary to continue the research in Japan, which would be carried out by the Japanese together with Indonesian young scientists to keep up the technology and science for the continuity of the research in Indonesia afterwards. The sending of those young scientists was listed into the exchange scientists program. They usually took with them the specimens which they wanted to study. In this way it was clearly seen that their skill in research and knowledge could be admirably lifted up despite the short training in Japan which lasted only 2 or 3 months or over. Another advantage was also gained in the improvement of undergraduate educational program. However, the exchange scientists program was not only used for sending those who dealt merely with research work, but also those who worked for the development of the institution. The development of the institution was put into the program so as to add the efficiency of a department in keeping up with the delopment in science and technology because of the invention of new equipment or method. Afterwards in the teaching program could also be improved.

During the 6 years joint research project they carried out several programs consisting of: 1. Dengue haemorrhagic fever, 2. Perinatology, 3. Hepatitis and hepatoma, 4. Diabetes mellitus. Now the joint research has been successful in its achievement to provide manpower or scientists who can improve their ability in research working so that they are much more capable in diagnosis or management of those diseases. The advantage of the joint research project can also be seen that the sending of the Indonesian staff to Japan can be more directed to the needs which are felt in Indonesia. The facilities can also be added so that the result of the education can be directly used in Indonesia to avoid the frustration of them. Moreover, because of the generosity of Japanese scientists who are always aware of the additional needs in equipment and chemicals, they are not disappointed because they can develop their program and institutions.

Ronpaku program: By the acceleration of the exchange scientists program to become Ronpaku program, the development of JSPS program can be felt more suitable for the needs in Indonesia so as to increase the number of staff whose quality is equal to that of the doctor degree holders. The performance of Ronpaku program generally also conforms with the needs in Indonesia. So the topics of the dissertations should agree to the problems coming out in Indonesia. This is possible because Ronpaku program is a sandwich program of which one part is done in Japan and the other is completed in Indonesia using the specimens found in Indonesia. Although Ronpaku has just produced only one person, we have been able to evaluate his achievement, so that he can lead one activity in Indonesia not only for the laboratory but also for the more extensive program, a national program. This can be done in Indonesia because of the addition of the equipment which could be obtained by the effort of the promotor through the Government of Japan. For all of this I wish to mention the name of Prof. Susumu Hotta whose name is well known by us in Indonesia. The procedure to obtain the equipment and instruments has also been done by Prof. Iwai of ICMR by contacting JICA. This cooperative organization in Indonesia has involved several universities such as, University of Indonesia in Jakarta, Gadjah Mada University in Yogyakarta and Airlangga University in Surabaya. Last year Padjadjaran University in Bandung began to participate.

Results of the first phase: As a result of the first phase cooperation, based on the number

of research staff, including those who are still in Ronpaku program, we have decided to establish 5 centers: 1. Dengue haemorrhagic fever, 2. Hepatitis and hepatoma, and 3. Tissue culture in Jakarta, 4. Perinatology in Yogyakarta, and 5. Diabetes mellitus in Surabaya. The establishment of those centers is decided to enable to pool the manpower, facilities and program so that the activities of research is done in those centers or coordinated by those centers. The Japanese or foreign scientists who would like to do research together in Indonesia can also stay in those centers. For the center of tissue culture which is located in the Department of Microbiology, Faculty of Medicine, University of Indonesia, I would like to say that the activities on cell fussion and DNA-recombinant will be intensified. The program can be done because of the result of Ronpaku program in virology from Kobe University and microbial genetics from Osaka University, which is helped by the other staff already existing, also from Department of Biochemistry, Department of Immunology and Biomedical Laboratory of the Ministry of Health with the NAMRU laboratory in Jakarta. This project called Medical Biotechnology Project which will be a subdivision of a net work of the National Project on biotechnology coordinated by the Institution for the Development of Science in Indonesia (LIPI) and the Ministry of Research and Technology. By this assignment we understand that the government acknowledges on the ability of Department of Microbiology which also means its acknowledgment on the program currently going on between Japan and Indonesia especially through JSPS coordinate by ICMR. This is the first step or embryo of a program which will really become one of the priority programs of the government to develop biotechnology.

In conclusion the cooperative program between JSPS and DGHE has participated in the manpower development of some universities in Indonesia. And on behalf of the core universities in Indonesia I wish to express my appreciation and thanks to the government of Japan through JSPS and ICMR on the smooth cooperation and understanding of each other so that all the programs arranged together can run smoothly for our mutual benefit. Finally, our hope is that this program of cooperation needs to be continued and possibility intensified.

4 JAPANESE AND INTERNATIONAL ORGANIZATION FOR MEDICAL COOPERATION

4a COOPERATION OF JAPAN INTERNATIONAL COOPERATION AGENCY WITH DEVELOPING COUNTRIES IN THE CONTROL OF TROPICAL DISEASES

YUTAKA HASEGAWA

Japan International Cooperation Agency, Tokyo

As of July 1985, JICA implements 34 health and medical projects to cooperate with developing countries, out of which 7 are related directly to tropical diseases. Non-tropical disease projects as well as other non-medical projects are mostly undertaken in tropical areas of developing countries, and therefore special arrangements have been made for Japanese experts engaged in the projects in such areas, in order to minimize health risks from tropical diseases. JICA plans to intensify its efforts to battle against tropical diseases including malaria. Brief accounts are given on the present state of the 7 tropical disease projects.

4b ACTIVITIES OF WHO AND JAPAN FROM THE VIEW POINT OF SOUTH AND NORTH PROBLEM

ISAO ARITA
Kumamoto National Hospital

WHO's major activities are now to coordinate the international cooparation in the area of health and medicine with focus on how prevent deterioration of health status in developing countires. There have been 3 WHO global programmes, namely the global eradication of smallpox, the expanded programme of immunization and the programme of tropical disease research and training.

The first programme has been successfully completed. All are heavily supported by the international cooperation. How Japan should contribute to the international cooperation through multilateral or bilateral assistance is discussed.

4c COOPERATIVE EFFORTS IN MEDICAL SCIENCES BETWEEN JAPAN AND SOUTHEAST ASIAN COUNTRIES

FUMINORI SAKAI
Executive Director, Japan Society for the Promotion of Science

The Japan Society for the Promotion of Science, which is called JSPS for short, is implementing cooperative programs for scientific exchange with 28 countries of the world. The cooperative activities cover all the fields of science, including humanities and social sciences. In the framework of these bilateral programs, JSPS pays special attention to the ways and means to promote close relations with Southeast Asian countries. Today I would like to talk briefly about the present status and the future prospect of cooperative activities, especially in medical sciences, which JSPS is developing with Southeast Asian countries. International programs of JSPS are aimed at contributing to the fostering of researchers for universities and research institutes. JSPS does not conduct research by itself, nor does provide support for facilities and equipments. It assists researchers in their scientific, and programs for students, such as scholarships, are not included in its mandate obligations.

JSPS programs which are conducted in compliance with its duty of training research manpower and of promoting international exchange of scientists are categorized into the following 4 types; 1) exchange of scientists, 2) organization of international seminars, 3) international cooperative research, and 4) dissertation research by foreign researchers wishing to obtain doctoral degrees from Japanese universities.

Asian countries with which JSPS is conducting cooperative programs are divided into two groups, according to the types of activities included in the cooperative programs, one group including Southeast Asian countries such as Thailand, the Philippines, Indonesia, Singapore and Malaysia, and the other group including China, India, Korea, etc. In the case of the latter

group, JSPS concludes agreements or memoranda of understanding with its counterpart agency or agencies in each country, and carries out exchange of scientists programs, sharing the expenses with them in the style where the sending side pays for international transportation and the receiving side covers the maintenance study trips in the host country. In the case of the former group, the financial arrangements totally differ from those of the latter group, because JSPS pays for all the expenses necessary for the implementation of the programs. JSPS and the counterpart agency in each country meet every year and decide the scope, priority, etc. of each program for the next year.

A. Past Achievements

1. Exchange with Southeast Asian countries

All the programs are carried out through negotiation with the agencies in each countries.

a) Exchange of scientists: We know that biomedical scientists from Southeast Asian countries who visited Japan during FY 1982 were 40 in total, making little difference from 53 of the United States and from 45 of the other countries including those in Europe. In contrast, however, it is known that corresponding numbers of Japanese scientists sent out during the year, given in the lower sections, were 33 to Southeast Asian countries, 119 to the United States, and 20 to the other countries including those in Europe. The number of exchange scientists are increasing, though little by little every year. However, numbers alone do not tell the real status of exchange programs. We should know at the same time how long each scientist was engaged in research activities in the counterpart country. Generally speaking, younger researchers tend to desire to stay a longer period (6 months to one year), and senior scientists, a shorter period. The duration of stay per a individual scientist shows a growing tendency.

b) Seminars and joint research activities: In the area of biomedical sciences, Kobe University which is designated as the core university on the Japanese side is responsible also for the organization of seminars and the arrangement of joint research activities. Activities in this regard are becoming more and more vigorous with the increasing number of participants from areas outside Southeast Asia.

c) Dissertation research by those desiring to obtain doctoral degrees from Japanese universities: JSPS implements a program with the purpose of supporting researchers from Southeast Asian countries in their dissertation research to obtain doctoral degrees from Japanese universities. It is a matter of course from its purpose that the target of this program is a researcher who, after accumulating considerable amount of research achievements, wants to make up his insufficient experimental data for the completion of the dissertation. The researcher, when accepted for the program, may stay in Japan and couduct experimental research under the guidance of his Japanese adviser for a period of from 2 to 3 months annually, while receiving continued guidance from his home adviser for the rest of the year in his home country. He is expected to complete his dissertation within a total of 5 years. JSPS pays for the necessary expenses for his travel and maintenance in Japan, regarding this program as most effective for the training of researchers who can play an active part in academic circles of their respective countries. At present medical researchers from Southeast Asian countries who are receiving assistance under this program are 12 in number.

2. Exchange with China, India and Korea

Exchange programs with China, India and Korea were established only several years

ago and, therefore, not a many researchers in biomedical sciences have been exchanged, a total of 12 foreigners being invited to Japan by FY 1981. A new program for receiving medical scientists from China was started from FY 1984, under which 6 scientists are invited to Japan annually.

B. Future Prospects

The advancement of medical sciences in a wide sense, including clinical treatments, will not be attained through relevant technical progress only. The technical progress should be accompained by the harmonious development of humanities and social sciences, not to mention the different fields of natural sciences. The treatment and prevention of diseases which constitute one of the biggest pains of mankind is the ultimate purpose of the medical sciences, but every field of sciences has to do with it. Another factor which I regard as more important is the part to be played by efforts and activities of the native people of this district who are well equated with their local environments. Just the financial or institutional provision is not enough for the accomplishment of the object. We who are involved in the efforts for medical advancement should not stick short-sightedly to technical issues, but stand on a wider field of vision and extend the utmost cooperation so that the human health in each of the Southeast Asian countries will be improved and better promoted.

5 MEDICAL COLLABORATIONS WITH TROPICAL COUNTRIES

5a INTRODUCTORY REMARKS

AKIHIRO FUJIOKA[1] AND MORIYASU TSUJI[2]

Internal Medicine, Hyogo Prefectural Amagasaki Hospital[1] and Department of Parasitology, Hiroshima University School of Medicine[2]

For the cooperation with tropical countries, medical and clinical projects are situated in important. However, these medical and clinical projects should be done along the actual conditions of each countries. All of symposists in this session have the practical experiences of medical research or clinical services in Southeast Asian, Central and South American and/or African countries. It seems to be that the important diseases for health problems among each countries are different between progressing areas such as Southeast Asia and Central and South America and several African counries. Time is not enough to speak all, but we expect that all symposists shall explain about these problems from their past experiences from medical view points. And we hope this session would be useful for our future cooperations with tropical countries.

5b MEDICAL AND THERAPEUTICAL COOPERATION WITH TROPICAL COUNTRIES

KIICHI SATO
Institute for Tropical Medicine, Kanazawa Medical University

Generally speaking, there are two aggressive ways of medical cooperation for the tropical area: (1) the cooperation of our own people going to the country in question for aid, and (2) secondary one of inviting those who want to undergo trainings in Japan from the developing countries.

As for the former, in the relation of a single or a few doctors from our side against lots of natives, we must be obliged to make much more efforts than we can imagine, including the problem of language and so on. On the contrary, concerning the latter, quite the reverse, we have received comparatively good evaluations until now because several problems can be managed by the people arround.

Incidentally it is inevitable to be affected with the social and economic restrictions. In a case of the above (1), as is the work in "shortage of goods" or "poverty", we sometimes use the old ones or recycle the used, and, in the worst case, are compelled to do with surrogates. In a case of above (2), training in the abundant circumstances as it is, there occurs a doubt whether the acquired or mastered techniques and knowledges can be applied effectively after trainees' return. As a result, the urgent request for instruments will be submitted to our government.

Considering the above, each way has both advantages and disadvantages. It seems quite difficult to make up a satisfactory medical cooperation. The author, having being touched the both and keeping on, show here some experiental cases.

Experience 1: Autopsy of lassa fever (1974); When this author was in Nigeria University Teaching Hospital, Enugu, Nigeria through JICA cooperation, he had to perform a autopsy of a patient (Germany doctor, 29 years old) who sufferred with the dangerous infected lassa fever, because of the neglect of university staff. After then, however, the university staff understood well, and became willing to do anything, if it was necessary.

Experience 2: Ear surgery camp in Thailand; It was reported that about 80,000 patients with chronic otitis media were present in Thailand. Several voluntary otolayngological doctors had taken part in clinical examination and treatment for the patients. The author has been concerned with this voluntary action since 1981, for coworking with operation of the ear infection. He wants to express that our country should help them by providing the medical equipments and transports at this time. Because, almost all of the medical equipments were Japanese products and became very old.

Experience 3: Medical educational cooperation with YARSI Medical School, Jakarta, Indonesia; Since 1982, our university is keeping and continuing the educational cooperation with the above medical school by our own sponsorship. We have the combined annual symposium on the big theme of tropical medicine. And also, the author visited there to give the condensed lectures to YARSI students, about 3 weeks per year. On the other hand, our university invited 4 medical doctors from YARSI staffs and suport their research works in the postgraduate course. These exchange will result in the fruitful cooperation, in near future.

As the conclusion of medical cooperation, the author wants to emphasize the importance of how to supply and how to improve the disadvantage of each cooperation. And the people who concerned with cooperation have to know what kinds of problems are present in each programme. The auther thinks that it is better to find these problems as early as possible for the establishment of good humanity.

5c TECHNICAL COLLABORATIONS PARARELLED WITH GRANT-AID PROGRAMME

MAMORU SUZUKI
Department of Parasitology, Gunma University School of Medicine

To date, Japan has promoted Grant-Aid-Programme to assist malaria control projects in 6 endemic countries. Subcommittee on malaria control of the Overseas Medical Cooperation Committee had examined the past programme worked by Japan International Cooperation Agency and stressed the importance of technical collaborations which should be worked in association with donation under the category of Grant-Aid-Programme. Overseas Medical Cooperation Programme needs experts of long-term appointment in the involved countries. However, recessing number of staffs in the Government Institutions including University Departments has caused difficulties to carry out the cooperation in the control of malaria in tropical countries. Regarding such envisaged situations at present, some breakthrough should be devised to have smooth collaborations with counterpart experts. In the past experiences in Haiti and Sudan, we would propose relatively easy approaches which should be taken into consideration to join successful technical collaboration to donation. In both countries, several laboratory items were included in the original request, and our Government admitted them. When the programmes were taken into actions and laboratory items were arrived to the places, counterpart government sent another request asking for technical experts to assist them to install laboratory instruments such as fluorescence microscope, freezer, refrigerator, centrifuge and so on. Taking these opportunities, workshop courses were held to instruct technical principles to carry out indirect fluorescence antibody test and drug resistance test. The counterpart governments again sent requests to accept trainees in Japan in the appropriate institutes to deepen their knowledges and master further technical details so that they can carry out laboratory works using donated laboratory instruments. Thus, within the limit of already existing categories, a kind of technical collaborations were successfully worked. Such collaboration systems will also provide excellent opportunities to test some new techniques which were developed in Japanese research institutions. In this regard, we are to test applicability of a new drug resistance test on *P. falciparum* by a fluoro-assay system which we consider can be recommended in the laboratories in the tropics.

5d ACTIVITIES OF JAPAN MEDICAL TEAM FOR DISASTER RELIEF

TAKASHI UKAI
Osaka Prefectural Senri Critical Care Medical Center

Types of international medical cooperation can be classified into 3 categories by the grade of their urgency. One, such as emergency medical relief activities to the victims of disasters, is comparable to "acute" diseases to which emergency response is indispensable. Another is "subacute" type such as control of epidemics in the certain limited areas. The other type is "chronic" or long-term one which include construction of hospitals or research laboratories, education of health workers, projects on the social hygiene, etc.

Efforts of international medical cooperation in Japan were mainly made on the chronic ones and acute or emergency cooperation were scarcely taken into account in the past.

In autumn 1979, when a great number of starved and wounded Cambodian people crossed the border into Thailand, many medical teams were dispatched to the refugee camps from various countries. In spite that this tragedy took place in Asia, Japan failed quick response to it, and went far behind the European countries and the United States.

The idea to establish an organization which enables quick reponse to overseas disasters was raised at the end of 1980, and was realized in March 1982. This is called Japan Medical Teams for Disaster Relief (JMTDR). Secretariat of JMTDR is placed in the Ministry of Foreign Affairs, Beareau of Technical Cooperation. Ministry of Health and Welfare, Ministry of Education, Japanese Medical Association, Japan Red Cross Society, Japanese Association for Acute Medicine and Japan International Cooperation Agency send representatives to the steering committee of JMTDR.

Routine activities of JMTDR are, (1) registration of volunteer medical workers, (2) storage of medical equipments and medicines, (3) holding training seminars and publication of news letters, (4) gathering informations about emergency medical cooperation, etc. By the end of September 1985, 261 medical personnels had registered to JMTDR.

In November 1984, when Minister of Foreign Affairs Mr. Shintaro Abe made a round trip to Africa, Dr. Kenji Honda, Chairman of JMTDR, accompanied him and made an inspection of a shelter of drought affected people in Mekelle, Ethiopia. According to his report, dispatch of JMTDR to Ethiopia was decided on November 30, 1984, and the first team left Narita Airport on December 10.

This team was the second medical team from abroad to Mekelle. Team members assisted Ethiopian medical staff to make field hospital in the shelter and treated about 200 outpatients and 100 inpatients in a day. Thereafter, 32 JMTDR members were dispatched to Mekelle until April 7, 1985. Though daily mortality in this shelter was about 30 among 20,000 population in the beginning, it fell to 0 to 1 at the end of March, 1985.

Second dispatch of JMTDR was to the big earthquake which assaulted Mexico city in the early morning of September 19, 1985. Through these 2 experiences we learned (1) it is quite important for the effective emergency overseas cooperation to have apporopriate means of transportation, (2) it is almost nonsense if JMTDR could not arrive at the site immediately, for example, in case of natural disaster like earthquake, time limit of arrival at the site is less than 48

hours after the catastrophe, (3) emergency relief activities should not be limited to medical help but should also be extended to over-all rescue activites, (4) JMTDR should have much more registered volunteers to strengthen its capability, (5) in order to execute the activities JMTDR smoothly, it is desirable to have preagreement between Japan and Asian countries on the dispatch of JMTDR.

5e OPHTHALMIC ACTIVITIES AT MALEKURA ISLAND OF THE REPUBLIC OF VANUATU

WAKAKO IWASAKI
Department of Ophthalmology, Kansai Medical University

As the means of indirect aid to WHO which is advocating "Development of Public Health and Hygiene in the South Seas Islands", we have practiced medical examination at schools and at Norsup Hospital as well as visiting patients at remote places Malekura Island (Population 12,000–17,000) which is the second largest island of the Republic of Banuatu. These activities took place for 3 months from April to July and one months from August in 1984, as a completely voluntary activity supported by cooperation of medical appliances manufacturers, medical supplies companies and doctors.

Medical examination were conducted by 4 Japanese ophthalmiater at Norsup Hospital and Lamap Hospital for 248 out patients, at other 10 local clinic centers for 194 patients, at 3 primary schools for 269 pupils which are summed up to 711 altogether, with 26 operated patients for 29 eyes operations. What is specially noteworthy was that pterygoid was found mostly were among twenties and that 4% of students were suspected to have trachoma while there was no trachoma symptom among the youth. In order to take positive part for the prevention of loss of eyesight in the the South Seas Island which is the objective of WHO, we have submitted the report concerning details of medical examinations at the above island. This is an additional report as the result of our consideration over the future problems.

5f COOPERATIVE STUDY BY INDONESIAN AND JAPANESE DOCTORS ON DENGUE HAEMORRHAGIC FEVER (DHF)

YOSHINORI FUNAHARA
Department of Physiology, Kobe University School of Medicine

The project team composed of pediatricians, hematologists, virologists and immunologists from Indonesia and Japan was organized in 1979 by the aids of JSPS, ICMR and DGHE to clarify the pathogenesis of the bleeding of DHF, and to make a protocol for the treatment of the bleeding. Since then, the project has been operated by getting some financial supports from Ministry of Education of Japan, JSPS, JICA, ICMR etc., and by having very good partners in the study. The obtained data during these 7 years were presented by Funahara *et al.* at the First

ICMR Seminar on Dengue and Dengue Hemorrhagic Fever (Kobe, Japan, 1980), the International Symposium on Disseminated Intravascular Coagulation (Tokyo, Japan, 1981), the International Conference on Dengue/Dengue Hemorrhagic Fever (Kuala Lumpur, Malaysia, 1983), the First International Seminar on Dengue Hemorrhagic Fever in the Americas (San Juan, Puerto Rico, 1985) etc. Based on the data reported, doctors in ASEAN countries are going to have a new project on the treatment of DHF in 1986.

For the operation of our project in Indonesia, the followings attentions were made:

1. Efforts were made to exchange our knowledge and techniques of medical science not limited in the field of DHF. As the results, Japanese scientists could have experiences to study cases which had been learned by only literatures. Good human relations, established between teachers and students during the exchange, made it possible to continue our projects without trouble for 7 years.

2. All specimens obtained from the patients were examined in the laboratories in the University of Indonesia. Therefore, it was possible to introduce newly developed techniques to many doctors not only of the project but also out of the one.

To set up a laboratory for the study, a room was prepared by the University of Indonesia, and some equipments were supplied by JICA. Three Indonesian doctors of the project were sponsored by JSPS to continue their study on DHF and related field in Japan. Thus, coming back from Japan, they could train the other doctors in Indonesia for the replacement of some role in the project which were done by Japanese doctors, and now the project can be operated if one or two Japanese doctors who consultate with Indonesian doctors on the study can join, and some reagents are supplied to the project.

5g THE TRIBHUVAN UNIVERSITY MEDICAL EDUCATION PROJECT IN NEPAL

SANAE KANDA[1] AND TADA-AKI IWASAKI[2]

Department of Anatomy[1] and Internal Medicine[2], Hyogo College of Medicine

The master plan of the technical cooperation programmes concerning the Tribhuvan University Medical Education Project was presented in June, 1980, and the Nepalese and Japanese delegations were in agreement with the plan. The principal objects of the plan are listed as dispatch of the Japanese experts to Nepal, the supplies of equipments and training of the Nepalese experts in Japan, and it purposes to fostering of medical doctor in Nepal and desire a level up of medical practices or educations. This technical cooperation covers during 5 years and the duration is divided in 2 parts: the first period is completion of medical school (1980–1982) and the second period is construction of teaching hospital (1983–1984).

Dispatch of the Japanese experts to Nepal purposes technical transfer in Nepal and does not offer man-powers.

The laboratory equipments are supplied in the first period and the clinical equipments are in the second period of the cooperation. Three hundred million yens are appropriated to the supplies of equipments during 5 years. The training of the Nepalese experts in Japan are scheduled as 30 persons at the starting point of the cooperation, and reception facilities of the

experts is the Hyogo College of Medicine.

Construction of the teaching hospital is managed by the Japanese Grant Aid Programmes.

The points in question of the technical cooperation are cited that the requests of the Japanese experts are not presented from the Nepal side and Nepal desires offering of man-power in long periods.

Fifteen Nepalese experts were accepted for training in Japan during the past 5 years.

Another questions are the prohibition of medical practices of foreign doctors in Japan and speaking of Japanese.

The teaching hospital in Nepal was completed in March, 1985 and managements of the hospital was transferred to Nepal side. The technical cooperation expired also in 1985 but the new cooperation was extended for 3 more years. The questions in coming period are transportations and maintenances of equipments, supplies of educational implements and wasting materials.

An active dispatch of Japanese experts and trainings of community physicians in Nepal are desired in the future.

5h JAPANESE COOPERATION FOR MEDICAL EDUCATION THROUGH THE RESEARCH INSTITUTE FOR TROPICAL MEDICINE IN THE PHILIPPINES

TADASU NUNOUE

School of Health Sciences, Kyushu University

In the Philippines, high morbidity and mortality due to communicable diseases have been the most important impact to the nation's health. Some projects were performed to control malaria, schistosomiasis, tuberculosis and cholera. Japanese researchers also cooperated respectively to each project. In April 1981, the Research Institute for Tropical Medicine (RITM) was inaugurated, which was a biginning of synthetic research for tropical and infectious diseases. The RITM was constructed with modern facilities and equipped with sophisticated instruments by cooperation of Japan through the JICA. The government of the Philippines supports financially to maintain the institute. Biomedical, clinical and/or operational researches are ongoing in the fields of acute respiratory infections, diarrhea, schistosomiasis, meningitis, hepatitis, malaria, leprosy and filariasis. Laboratory works spotlighted many pathogens; bacteria, protozoa and viruses including dengue. These progressive and scientific data are the requisite for prevention of communicable diseases. The RITM has clinical department which contributes to health care for local residents and at the same time to research strengthening. In the both clinical and research departments, rotating residents and fellows from the affiliated hospital including UP–PGH engage in training for infectious diseases. The rural health practising physicians are also trained for public health. Medical technologists are able to receive training in the special course, for example, of electron microscopy. These programs for manpower development are included in part of institutional strengthening activities. Japanese specialists have participated in the activities of the RITM, in the fields of feasible research areas and manpower development successfully. Techniques to be transferred should be economical and productive in local base.

Development of and support to the specialists who understand essentials of the cooperation locally required, are responsibility of Japanese authorities to the developing countries.

Infectious diseases of international travelers in the tropics -present status of epidemiology and control

1 INTRODUCTORY REMARKS

TOSHIO NAKABAYASHI[1] AND TAKAKAZU AOKI[2]
Research Institute for Microbial Diseases, Osaka University[1]
and The Infectious Disease Center, Osaka Momoyama Hospital[2]

Recently, oversea travelers and foreign visitors to Japan have greatly increased in number. Travelers in the tropics have also had increased chances of being infected with diseases of various origins; viral, bacterial, protozoan and parasitic. In this symposium, infectious diseases of particular importance for international travelers in the tropics will be presented by several experts with special focus of epidemiology and control measures.

2 THE CURRENT STATES OF IMPORTED DISEASE AT THE INFECTIOUS DISEASE CENTER, OSAKA MOMOYAMA HOSPITAL

TAKAKAZU AOKI
The Infectious Disease Center, Osaka Momoyama Hospital

Since the beginning of 1974, the studies on imported diseases in inpatients at our center have been done and reported successively. Almost all of these patients were returning-travellers suffered from acute infectious diseases, so-called "travellers diarrhea", FUO (Fever of Unknown Origin) and jaundice.

Recently, these imported diseases at our hospital are changing into infectious diseases resembled to the "United Kingdoms type". For this reason, the numbers of these imported diseases inpatiants travelled as "Treking" in the rural districts to Indian Subcontinent and African Continent. The current states of imported diseases in returning-travellers were presented.

3 INTERNATIONAL INFECTIOUS DISEASE — LASSA FEVER, MARBURG DISEASE, EBORA HAEMORRHAGIC FEVER

YATSUKA IMAGAWA

Department of Infectious Disease, Tokyo Metropolitan Bokuto Hospital

"International infectious disease", which is the administractive term dealing with a patient in Japan, is indicated of lassa fever (LF), marburg disease (MD) and ebora haemorrhagic fever (EHF) and LF is regulated under the infectious disease prevention law.

Occurrence: LF is exist in West Africa (Guinea to Central Africa), MD in East and South Africa and EHF in Zaile, Sudan, Central Africa Republic and Kenya. Except for Africa, LF was occurred in 10 cases (2 cases died) in England, 3 cases in America (laboratory acquired infection of 2 cases and 1 death), each one case in West Germany, Netherlands and Australia. These were not secondary infections including transportation but imported cases. There was no occurrence of MD except for the incidense of secondary infection (7 died out of 31 cases) caused by imported African green monkey from Uganda on West Germany and Yugoslavia in 1967. There was one laboratory acquired infection with EHF in England.

Animal reservoir and transmission: It is confirmed that LF is carried by *Mastomys natalensis* inhabiting widely at the area of Savanna and the virus is excreted from urine and saliva. MD and EHF are suspected that they are carried by rodents but yet unconfirmed. On the infectious route to human, it is mainly through needle stick or other penetrating injury with the patient's blood or excreta but is possible to aerosol infection by a close contact with severe patients.

Clinical symptoms and differential diagnosis: These diseases belong to the viral haemorrhagic fever, and their attacks started with non-specific symptoms like influenza. But there is no conclusive factor in the clinical diagnosis of these diseases. The diseases to be differentiated are malaria and typhoid fever.

Viral diagnosis: It becomes problems on dealing with the patient and the contact in cooperation with long incubation period (the longest is 17 days in LF) and the illness day of virus isolation from blood (LF in 19, MD in 15, EHF in 8), urine (LF in 32, MD in 7), pharynx (LF in 19, MD in 6), semen (MD in 83, EHF in 61).

Prevention and treatment: Arenavirus, which was separated from *M. natalensis* at Mozambique in 1977, showing close immunological cross reaction with lassavirus, have weak infectious ability to monkey, and is effective for prevention of attack in LF with monkey. It is expected that Ribavirin could be also effective against LF with monkey by the future development.

Caution for travelers: In England in 1982, there were found 44 cases of viral haemorrhagic fever after return from Africa, and 2 cases were confirmed as lassa fever. It proved experimentaly that the man, who engage in the local hospital, various researches and projects at the rural area.

Management in Japan: As the accomodations of patients in Japan, there are a high security ward with isolater and clinical laboratory in Tokyo Metropolitan Ebara Hospital, a examination institute on virology in National Institute of Health and transit isolaters in each Narita and Osaka

Airports and Tokyo Metropolitan.

4 VIRAL HEPATITIS IN TROPICAL AREAS

TOSHIO SHIKATA
Department of Pathology, Nihon University School of Medicine

Several hepatitis viruses cause viral hepatitis in human beings. Clinical symptoms and histological features are quite same between various hepatitis caused by different viruses, such as, hepatitis A virus, B virus, δ virus and non-A, non-B viruses. Hepatitis A and one kind of non-A, non-B hepatitis virus only causes acute hepatitis by transient infection, whereas, hepatitis B and other non-A, non-B viruses cause not only acute hepatitis but also chronic hepatitis, liver cirrhosis and hepatocellular carcinoma by persistent infection. Prevalance of hapatitis A is very high in tropical areas and prevalance of hepatitis B is high in Asian-African countries.

5 BACTERIAL ENTERIC INFECTIONS

YOSHIFUMI TAKEDA
Department of Bacterial Infection, The Institute of Medical Science,
The University of Tokyo

Epidemiological study at Osaka Airport Quarantine Station shows that the most prevalent bacterium causing traveller's diarrhea in oversea travellers in our country is enterotoxigenic *Escherichia coli,* followed by Salmonellae and *Vibrio parahaemolyticus.* About 90% of traveller's diarrhea caused by bacteria are due to infections of these 3 bacteria. Compared with these, rates of isolation of Shigellae and *Vibrio cholerae* are very low, but these 2 bacteria are important in tropical countries. Also these 2 bacteria, should be handled with special care as these are controled by a law in our country.

Present global pandemic of cholera has been mainly due to *V. cholerae* biotype eltor. However, *V. cholerae* biotype classical has reappeared in Bangladesh in the autumn of 1982. It would be possible that classical *V. cholerae* might spread out of West Bengal to other areas of the world in future.

Importance of enterotoxigenic *E. coli* as a causative agent of traveller's diarrhea has been recognized since around 1975. It has been reported that about 20–25% of patients of traveller's diarrhea in our country are due to enterotoxigenic *E. coli.* Sporadic diarrheal cases and food poisoning due to enterotoxigenic *E. coli* have also been reported.

Oral rehydration therapy, recommended by World Health Organization, which has been becoming popular in developing countries, is not applied to patients of traveller's diarrhea in our country. Since the oral rehydration solution is easy to handle for oversea travellers, the knowledge and advantages of oral rehydration therapy should be advocated in medical society.

6 ON MALARIA

SUEHISA TAKADA
Department of Medical Zoology, Osaka City University Medical School

Owing to the effort of MEP (Malaria Eradication Programme), marked reduction of malaria morbidity and mortality had occurred on a world wide scale, and the objective of malaria eradication had been achieved in more than 20 countries or areas by year 1970. However, since the late 1960's the malaria situation had progressively deteriorated in many tropical countries and in some countries the malaria resurgence had shown epidemic situations in the middle of 1970's. According to the information of WHO, in 1983 more than half of the world's population-some 2,616 million people (56%)-lived in the malaria endemic area, and about 389 million people (8%) inhabit areas where no specific measures are undertaken to control malaria transmission and where the prevalence of infection has hardly changed. Thus in endemic countries, malaria threaten not only the health of inhibitants but also the socioeconomic development of the communities, and in malaria free countries the increasing cases and deaths of imported malaria from endemic areas are annoying problems.

At present malaria parasites are developing resistance to the antimalaria drugs, and the vector mosquitoes are becoming resistant to DDT and other insecticides. Behavioural changes of vector mosquito, such as avoidance of contact with insecticide sprayed wall, are also serious problems in malaria control. Against the serious resurgence, in the middle of 1970's WHO has revised the antimalaria strategy from Malaria Eradication Programme (MEP) to Malaria Control Programme (MCP) and defined technical and operational approach to malaria control, and in 1978 WHO recommended the inclusion of antimalaria campaigns in national health programme or primary health care. Four tactical variants were also recommended to choose the most suitable and feasible combination of control methods in each endemic country.

Annual WHO reports, on world malaria situation and on malaria risk in international travel, are quite useful informations for us to guide the travellers how to prevent this disease. On the other hand, basic and applied researches for malaria control were encouraged and supported by WHO during past 20 years and are obtaining various creditable results. Recent report of 6 deaths from severe cutaneous reactions in American travellers who were taking Fansidar with chloroquine for chemoprophylaxis of *P. falciparum* infection has embarrassed us greatly (Wkly. Epidem. Rec. 60, 181, 1985; MMWR. 34, 185, 1985). Both WHO and CDC in USA have recommended judicious use of chemoprophylactic drugs for prevention of malaria infection in travellers to endemic areas. Although we not yet have such severe cases in Japan, considerable numbers of Japanese travellers to malarious areas are suspected to be using Fansidar or similar drugs.

For prevention of malaria infection in Japanese travellers, it is urgently requested in Japan to establish an organization which is responsible for planning the suitable method for malaria prevention, follow up survey of travellers to malaria endemic areas and for collection of accurate data of imported malaria cases in Japan.

7 PRESENT STATE OF TROPICAL PARASITIC DISEASES IN VIEW OF THERAPEUTIC DRUGS

YOSHIHITO OTSUJI

The Second Department of Internal Medicine, Faculty of Medicine,
Kagoshima University

As an interchange of personnel between Japan and foreign countries becomes more frequent so-called importation of tropical diseases has turned up as an important issue to be solved. In our country, on the other hand, difficulty to obtain therapeutic drugs for the tropical parasitic diseases has became a serious problem. In order to improve the situation a task force for studing therapeutic drugs for the imported tropical diseases was formed and means of procurement, safekeeping, dispensing, treatment effects and side effects of the drugs have been investigated.

Results accomplished during 1980–1985 are: 1) The drugs have been forwarded on request to medical institutions on 506 occasions covering the whole country. 2) Breakdown of the imported diseases revealed 144 malaria cases at the top on the list, followed by 119 strongyloidiasis, 40 trichocephaliasis, trichinosis, clonorchiasis, carinii pneumonia, latum diphyllobothriasis, amebic dysentry and lambliasis, in that order. 3) Drugs that have been in great demand are thyabendazole, primaquine, fansider, mebendazole, praziquantel and quinimax. 4) Medical institutions that have been in need of the drugs were university hospitals on 191 occasions, national and other public hospitals on 164 occasions and private hospitals on 52 occasions. 5) There have been 176 cases of imported parasitic diseases with 133 malarial cases topping the list followed by 13 strongyloidiasis, 11 chlonorchiasis, 9 lambliasis in addition to trypanosomiasis, schistosomiasis japonica, urinary schistosomiasis (Bilharz), trichinosis and saginata taeniasis. 6) There were 133 malarial cases with 103 Japanese patients and 30 foreigners. Age distribution of the patients showed higher incidence among younger generations with 55 cases among those in thirties and 46 in twenties. The malarial cases included 67 vivax, 32 tropical, one malariae and 3 unknown species malaria cases. Places of malaria infection for Japanese travellers were Asian region (45 cases), African region (42) and Oceanian region including New Guinea (14). We could not, however, trace original places of infection for 2 cases.

It has been keenly felt that issues of imported tropical parasitic diseases and realization of being able to procure therapeutic drugs in need without delay should be given utmost attention.

JAPANESE JOURNAL OF TROPICAL MEDICINE AND HYGIENE

Vol. 14 No. 2 June, 1986

CONTENTS

Published by

JAPANESE SOCIETY OF TROPICAL MEDICINE

c/o Institute of Tropical Medicine, Nagasaki University
12–4 Sakamoto-machi, Nagasaki 852, Japan