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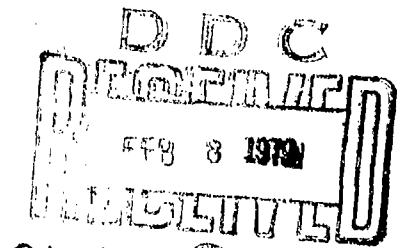
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ON THE TROPICAL MEDICINE RESEARCH TEAM;
OBSERVATIONS IN INDONESIA

Richard J. Brown and Peter L. Joseph

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November 1978

NAVAL AEROSPACE MEDICAL RESEARCH LABORATORY
PENSACOLA, FLORIDA

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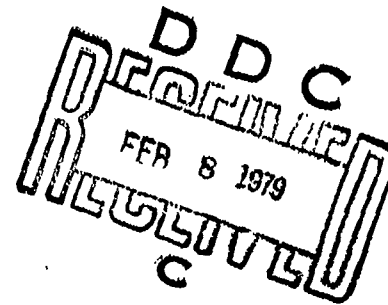
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SUMMARY PAGE

THE PROBLEM

In areas where public health and sanitary conditions are such that man comes in frequent daily contact with animals in his environment, rodent-borne human diseases are an important health hazard. Because of the year-round warm, humid climate in the tropics, inhabitants of such areas spend a considerable portion of their time out of doors. In tropical nations, such conditions are conducive to less than optimal health conditions; frequently the environment is contaminated by animals and their excreta. In such tropical areas of the world, a major portion of the preventive medicine efforts is involved in the identification of rodent-borne human diseases. Consequently, the experience of a veterinarian in rodent diagnostic and field laboratory studies makes him especially well suited as a member of the tropical medicine team to investigate these hazards.

FINDINGS

Many areas of the Republic of Indonesia were surveyed for animal diseases transmissible to man. These include schistosomiasis, scrub typhus, filariasis, capillariasis, and leptospirosis. All of these zoonotic diseases were present in this vast archipeligo.

ACKNOWLEDGMENTS

A close working arrangement was maintained between the U.S. Navy laboratory and the Indonesian Ministry of Health. The authors wish to thank Dr. Koesharjono, Chief of the Zoonoses Section of the Communicable Disease Section, who was the veterinary medical counterpart for the American veterinary pathologist. The authors wish to express their gratitude for the close working relationship with several other Indonesian veterinarians, including Dr. Iwan Budiarso, veterinary pathologist, Dr. Ikin Mansjoer, and Dr. Harjono.

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INTRODUCTION

The veterinary pathologist plays an important role as an integral part in the multi-disciplinary team approach to medical research in the tropics. He is able to provide unique services as a member of this team because of his training in both clinical and anatomic comparative pathology and a broad exposure to parasitology in veterinary medical school. Many animal diseases transmissible to man encountered in the tropics are diseases carried by ectoparasites that spend at least a portion of their life cycle on rodents. Collection and examination of wild rodents provide useful sentinel information on such rodent-borne human diseases.

A survey of tropical rodent-borne human diseases involves the trapping and proper handling of wild rodents, predominantly rats. Experienced animal trappers, under the veterinary pathologist's direction, bait and set usually one hundred traps per night in a given geographic study area, which generally covers two to five acres. These acres may be in and around houses in native villages, in fields where native crops are grown, or in areas of short scrubby undergrowth. The traps are collected early the following morning and taken immediately to a field laboratory where processing begins. The trapped rats are numbered, identified as to species, and transferred from their traps to a muslin bag; then they are anesthetized by dropping an ether-soaked cotton ball into the muslin bag. The anesthetized rats are bled and the harvested sera frozen for serologic studies. Tissues are removed at necropsy from the animals and fixed in 10 percent neutral buffered formalin for histopathology studies.

Tropical zoonotic diseases studied in Indonesia included schistosomiasis, scrub typhus, filariasis, capillariasis, eosinophilic meningitis, and leptospirosis.

PROCEDURE

DISEASE ENTITIES

Schistosomiasis

The major focus of Schistosoma japonicum studies in Indonesia was in the Lake Lindu area of central Sulawesi (Celebes). These studies included a description of the pathology of the Lindu strain of Schistosoma japonicum in the experimentally infected crab eating macaque, Macaca fascicularis. Several hundred fresh cercaria were obtained from the snail, which is the intermediate host, and exposed percutaneously on the monkey abdomen. The animals were examined histopathologically after 6 months, and the lesions were compared with the pathology in man caused by this strain of Schistosoma japonicum.

Scrub Typhus

Scrub typhus is a rickettsial disease caused by Rickettsia tsutsugamushi and is seen frequently in the tropics (8). It is transmitted to man by the bite of the six-legged chigger of the mite Trombicula deliensis which lives on wild rats. The isolation and

identification of the trombiculid chigger were accomplished by a group of technicians in the main acarology laboratory in Jakarta, also under the direction of the veterinary pathologist. After the animal trappers returned to the laboratory with the trapped rats, the acarology technicians carefully combed the anesthetized rats while observing them under a dissection microscope. Trombiculid mites, the carriers of scrub typhus, harvested from the same species of rats in the same geographic location, were pooled together and injected intraperitoneally into a group of five white laboratory mice. Approximately 3 weeks later, the spleens from these mice were harvested and passed a second time intraperitoneally into another group of white laboratory mice. After approximately another 3 weeks, the second passage mice were challenged with a known concentration of Rickettsia tsutsugamushi organisms. Immune white mice that survived the challenge were considered to have been inoculated initially with infected material collected in the field, and were thus considered positive for scrub typhus for their respective species of wild rat in the location under study. Mice that did not survive the challenge were considered negative for scrub typhus for their respective rat species in the location under study.

Spleens from the positive second passage mice were forwarded to more sophisticated infectious disease research centers for further confirmation. Tissues from all the trapped rats and experimental white mice were submitted to the veterinary pathology laboratory for histopathologic evidence of scrub typhus. In a few cases, such positive animals showed myocarditis, kidney perivascular mononuclear cell accumulation, peritonitis, and lymphadenitis. The ultimate purposes of scrub typhus work in Indonesia was to develop a vaccine for use in man and to identify suitable geographic areas for vaccine trials, as well as investigate the possibility of impregnating clothing with parasite repellent agents.

Filariasis

Reports of an unusual highly endemic form of filariasis from the Indonesian islands of Flores and Timor prompted a portion of the tropical research team to travel to this lower archipelago island in several instances for investigations. Uninfected healthy mosquitoes were allowed to feed on human patients infected with the Timor strain of filarasis. These mosquitoes, harboring a microfilaria undergoing metamorphosis, were transferred back to the main laboratory in Jakarta. Here, the mosquitoes, harboring infective larvae, were emulsified and injected subcutaneously in the medial femoral area of experimental Macaca fascicularis (crab eating monkey) and domestic felines.

Frequent nocturnal examination of the blood of these laboratory animals demonstrated the presence of circulating microfilaria. When the incubation period of the filarid neared its end, the laboratory animals were transferred to the main laboratory in Taipei where personnel of a sophisticated, well-staffed parasitology laboratory harvested and identified the adult nematodes. Subsequent study revealed this to be a previously undescribed human filarid, tentatively called Brugia timori. Identification of this highly endemic area afforded parasitologists and clinicians an opportunity to study a new filarid infestation in its natural habitat. In the future, this will provide an area for evaluation of the effectiveness of treatment with antifilarial drugs on populations with known prevalence rates. Determination of post-treatment prevalence rates will provide evaluation

of the effectiveness of drugs on this new filarid parasite. The availability and presence of pathology-free felines and nonhuman primates provided the necessary biological isolation mechanism for the discovery of this new human pathogen in the tropics (7). Additional Indonesian studies of the bancroftian filarid utilized pathogen-free hamsters and gerbils to recover various larval developmental stages.

Capillariasis

The common liver worm of rats, Capillaria hepatica, is widespread throughout the Pacific. The adults inhabit the liver of rats, and frequently large numbers of eggs will cause extensive hepatocellular necrosis and cirrhosis. Capillaria hepatica as well as Capillaria philippinensis are both human pathogens. Histopathologic examination of sentinel animal livers, collected throughout Indonesia, revealed the presence of Capillaria hepatica in both wild rats (6), house shrews (Suncus murinus) (4), and bats (Cynopterus brachyotis) (5). Although capillariasis has never been reported in man in Indonesia, it should be considered as a potentially pathogenic zoonosis in this archipelago.

Eosinophilic meningitis

The cause of eosinophilic meningitis in man is the rodent lung worm, Angiostrongylus cantonensis, reported to occur throughout the islands of the Western Pacific. Routine autopsy of sentinel animals included a careful systematic search of the lungs, and in Indonesia Angiostrongylus cantonensis was a common finding. Histopathologic examination of infected rodent lungs, revealing subacute eosinophilic pneumonia, corroborated these findings.

Leptospirosis

In the clinical pathology laboratory, examination of rodent kidneys for leptospirosis was conducted to determine the distribution of this disease in the study areas throughout Indonesia. Positive cultures were verified by hematoxylin and eosin routine tissue stains and by special leptospirosis stains.

LABORATORY COLONY

Other duties of the veterinary research pathologist in tropical areas included the establishment and maintenance of a pathology-free laboratory animal colony. Disease-free white mice were constantly required for scrub typhus surveys; nonhuman primates, hamsters, gerbils, and felines were utilized in filariasis studies, while guinea pigs were used as blood donors for blood meals for feeding mosquitos in human dengue research projects. Rabbits were used by several investigators for antisera production.

In a unique approach to the study of rodent-borne human tropical diseases, wild rodents that are known natural carriers of human diseases were colonized to a disease-free state. These disease-free rodents, which in nature are carriers of melioidosis, scrub typhus, leptospirosis, and other diseases, were exposed to the etiologic agents of these diseases to determine their antibody responses and thereby evaluate their future possible

roles as sero-epidemiological sentinels of human disease. This project required extensive trapping of wild rodents in Indonesia and shipping them to a suitably equipped laboratory for colonization to a disease-free state.

DISCUSSION

A significant amount of work has been accomplished in Indonesia, but there still remains opportunity for additional work.

A program of stray-animal control would be a significant step in the control of rabies. However, thousands of stray dogs have multiple owners in Indonesia, and capture and destruction of dogs running loose would bring a multitude of owners demanding indemnification from a very limited rabies control budget. Nationwide vaccination programs are difficult to conduct and enforce since Indonesia is comprised of hundreds of islands scattered over thousands of square miles.

Additional food sanitation studies need to be accomplished in Indonesia. A recent food poisoning outbreak in Banyuwangi in East Java caused the death of sixty-five people, and hundreds more became ill from eating a soybean-meat dish called Tempe. In Irian Jaya (Indonesian New Guinea), local health officials requested assistance of the American veterinary pathologist in Jakarta regarding sudden death of natives following consumption of poorly cooked pork. Laboratory samples were not submitted, only a history. Follow-up field work in this instance needed to be accomplished, but the great distances involved and financial constraints prohibited further study.

Melioidosis, a zoonotic tropical bacterial disease carried by rats and caused by Pseudomonas pseudomallei, occurred among Americans in the Vietnam War (10). The disease was reported in the 1930's by the Dutch in Indonesia (3) and in recent years has been found in Malaysia (1), to the northwest of Indonesia, and also in Australia (9), to the southeast of Indonesia. Recently an American visiting Indonesia died of melioidosis shortly after returning to the United States, in spite of antibiotic therapy (2). A survey to determine the prevalence, distribution, and antibiotic sensitivity of melioidosis is an area of opportunity for study along this vast archipelago.

It is not at all surprising that the veterinary pathologist finds a stimulating and satisfying role as a member of the tropical medicine research team. This is especially true in areas of the world where interest in tropical medicine research is on the increase, thus providing varied and imaginative opportunities.

COMMENT

A word is in order as to the excellent school facilities for school age children of Americans and other foreigners working in Indonesia. The Joint Embassy School in Jakarta is a large, very modern, first through twelfth grades, sponsored jointly by most foreign embassys in Indonesia. It consists of many octagon classroom buildings, each containing several classrooms, all connected by walkways lined with tropical flora. Here students from all corners of the world, including several iron curtain countries,

study and become friends together, completely disregarding international boundaries and political ideologies. Such a pre-college educational environment is truly an effective step towards promoting international good will and mutual understanding among the world's future leaders.



Illustration. Animal trappers preparing live catch traps on a recent field trip in East Java.

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