

SUMMARY
OF
CURRENT
RESEARCH



SEATO
MEDICAL RESEARCH LABORATORY
BANGKOK , THAILAND

THE SOUTH EAST ASIA TREATY ORGANIZATION

MEDICAL RESEARCH LABORATORY

BANGKOK, THAILAND

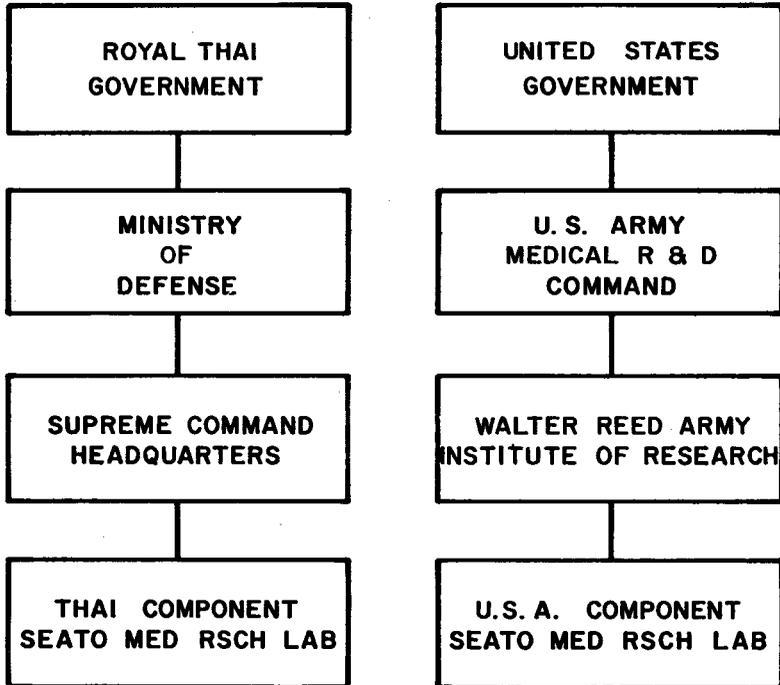
PREFACE

Disease and nutrition have influenced military campaigns throughout the history of the world. As late as World War II, battle decisions were influenced by diseases such as scrub typhus and dengue in the military troops. Certain areas of land mass were denied to military maneuver because of the overwhelming incidence of malaria. Today, malaria and other infectious diseases are better understood but are still diseases of major military medical importance. The soldier's abilities in combat are dependent upon his physical strength and endurance brought to a peak by training. The best training program and the most modern weapons will fail to achieve their objectives if the soldier is not physically and mentally capable of benefitting from them.

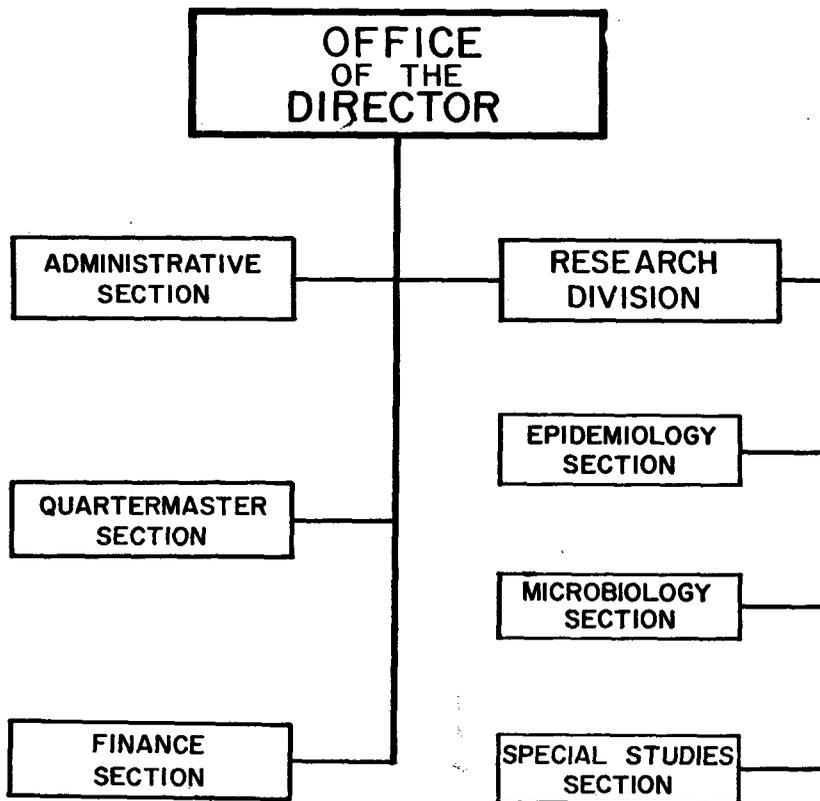


PUNG PHINTUYOTHIN
Major General, MC, RTA
Director General
SEATO Medical Research Project

**COMMAND CHANNELS OF THAI AND U. S. COMPONENTS
OF
SEATO MEDICAL RESEARCH LABORATORY**



ORGANIZATIONAL CHART
THAI COMPONENT
SEATO MEDICAL RESEARCH LABORATORY



UNITED STATES ARMY MEDICAL SERVICE

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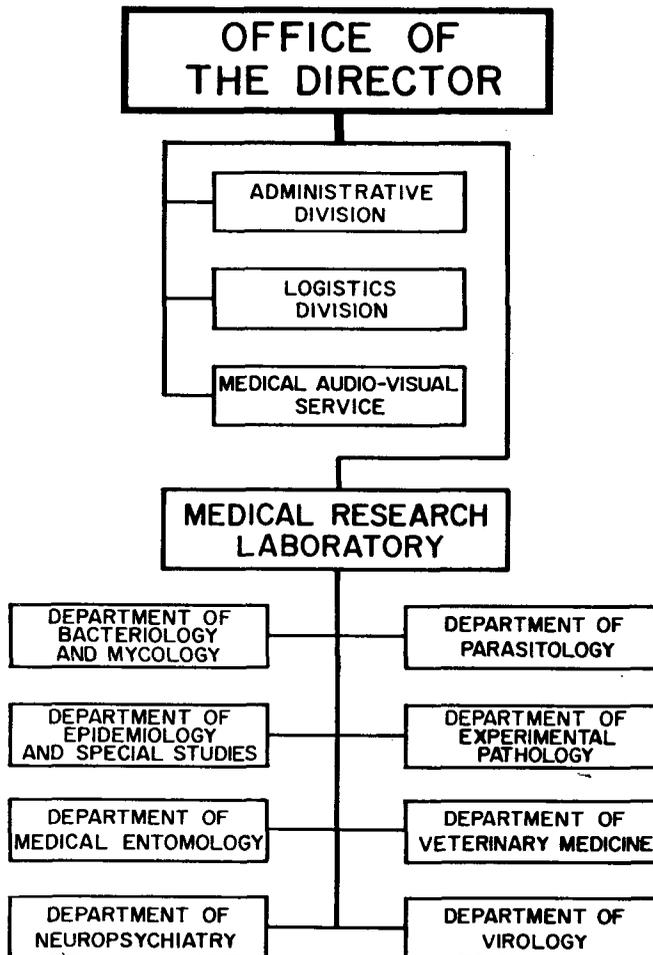


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PART I

BACKGROUND AND ORGANIZATION

At the 6th Council Meeting of Ministers in 1960 at Washington, D.C., it was proposed that the SEATO Cholera Research Laboratory in Thailand be converted into a SEATO General Medical Research Project and that other member Governments be encouraged to participate in it. The Thai and U.S. Components of the SEATO Medical Research Laboratory were established by an exchange of diplomatic notes between the Royal Thai and the United States Governments on 23 December 1960.

The mission is to conduct medical research, to assist with the education and training of medical and allied personnel and to provide special diagnostic laboratory facilities for patient care in cooperation with Thailand and other SEATO nations, for the benefit of all.

At present, the Royal Thai Government and the Government of the United States of America have contributed components which conduct independent studies and cooperative studies with each other and with other medical groups in Southeast Asia. From time to time other member nations send individual investigators to work here. It is hoped that other complete components will be added to the program in the future.

The components which make up the SEATO Medical Research Laboratory are under the Director Generalship of Major General Pung Phintuyothin, MC, RTA. The Thai Component of SEATO Medical Research Laboratory is responsible to the Ministry of Defense through the Director General, who is also Director of the

Thai Component and has served in this dual capacity since May 1961. The Deputy Director, Captain Samrit Jatinandana of the Royal Thai Navy was appointed in December 1962. The United States Army Medical Component, SEATO, under its Director, Colonel Marcus R. Beck, MC, is a special foreign activity of the Walter Reed Army Institute of Research.

The recent completion of the new Medical Research Laboratory by the Royal Thai Government permits centralization of most SMRL facilities which heretofore were dispersed in eleven buildings in various parts of Bangkok. Another new building to house the central laboratory animal colonies will be available in September 1968. An addition to the Medical Research Laboratory which will house the SMRL library and conference rooms and a new Plague Laboratory will be completed in early 1969. In addition to the main facilities in Bangkok, semi-permanent locations are established throughout Thailand as required. These presently include facilities in the North at Chiangmai, in the Northeast at Udornthani, in Central area at Phrabuddhabat, in the Southeast at Cholburi and in the South at Ko Samui.

The work of the three support services may be summarized as follows:

(1) Administrative Division--Maintains and prepares personnel and travel records and orders for U.S. and Foreign Service Local personnel. Prepares budget estimates, maintains informal accounting and a Cashier Fund. Operates medical library.

(2) Medical Audio-Visual Service--Provides still photography, photomicrography, motion picture, audio-illustrative, and reproduction support to the USA Medical Component, SEATO, and to the Walter Reed Army Institute of Research, Washington, D.C.

(3) Logistics Division--Transmits requests for supplies and equipment through Walter Reed Army Institute of Research to the depot system or to vendors. Procures supplies and services required which are available in Thailand. Operates a motor pool. Responsible for repair and maintenance of equipment. Provides janitorial service.

PART II

SUMMARY OF CURRENT RESEARCH

VIRUS AND RICKETTSIAL STUDIES

Arboviruses

A continual surveillance of dengue hemorrhagic fever and the causative agents is maintained. Extensive studies concerning etiology, epidemiology and control are being pursued. The relative roles of various Aedes species as vectors is being determined both by field studies and by laboratory infectivity and transmission studies.

The pathogenesis of hemorrhagic fever and the dengue shock syndrome are also being investigated. Evidence that severe manifestations are related to second dengue virus infections has been found. Further studies on sequence of immunoglobulin synthesis and serum complement alterations are in progress. An experimental model utilizing juvenile gibbons and monkeys is being developed to see whether the clinical syndromes can be duplicated in these primates, and to study the phenomena of repeated infections with antigenically related dengue viruses.

Tissue culture methods have been developed to implement all phases of arbovirus studies. By use of the delayed plaque technique a rapid and highly sensitive method has been developed for the isolation and identification of dengue, Japanese encephalitis, chikungunya, Sindbis, Tembusu and Wesselsbron viruses, all of which have been found to be present in Thailand. Plaque reduction techniques are utilized for the study of antigenic characteristics of these viruses; a micromethod is being adapted to the study of antibody prevalence.

The relation of arboviruses to human disease in Southeast Asia is being assessed. Human central nervous system infections in various parts of Thailand are studied in this regard. The occurrence of arbovirus infections in US military personnel in Southeast Asia is constantly monitored through cooperative programs.

A major study area at Bang Phra has been established to investigate the basic ecology of arboviruses in nature. The importance of birds, large and small mammals and other potential hosts is being studied, as well as parallel entomologic studies of mosquito vectors. Thus far the presence of virus of JE, chikungunya, Sindbis, Tembusu and Wesselsbron has been detected in this area.

Rabies

Rabies continues to be a disease of major importance in Thailand. It has been estimated that more than 400 cases of human rabies occur in this country annually. The program of rabies eradication includes extensive vaccination of animal carriers and elimination of reservoirs of infection. The Thai Ministry of Public Health has recently shown a renewed interest and effort in rabies control in outlying provinces by stray dog elimination and mass immunization programs. At SMRL efforts are being made to detail the prevalence and distribution of domestic rabies throughout Thailand. Virus isolates have been made from dogs, cats, cows, horses, and water buffalos. Wild-life reservoirs of rabies infection have not been defined. However, this laboratory has diagnosed bat rabies, and in some provinces where bats have been trapped the prevalence has been as much as five per cent. A recent survey of the rodent population in central and southeast Thailand has revealed that these animals have a significant degree of active rabies and could be a potential reservoir of infection.

During the calendar year of 1967 38.2 per cent of the 330 suspect specimens submitted to this laboratory were diagnosed as positive. Those positive included 3 humans, 121 dogs, 1 rat and 1 ox.

Respiratory and Enteric Viruses.

Current research programs are designed to assess the presence and relative importance of a wide variety of virus agents in the Bangkok area. The etiology of febrile respiratory disease is being determined in a large series of children. Special studies are initiated when necessary to investigate epidemic respiratory syndromes such as bronchiolitis or influenza-like illnesses. In addition, a study of the etiological agents involved in pertussis is in progress.

Acquired, presumably asymptomatic, cytomegalovirus infections of the respiratory tract appears to be very common in young children in Bangkok. The epidemiology and significance of these infections are being studied.

The occurrence of an extensive outbreak of rubella has prompted the study of congenital rubella infections as an expected sequela. Detection of such cases is being evaluated by screening cord sera of new-borns for fetal immunoglobulin synthesis. In addition, further studies of the immunological response in these infants is under way.

The etiology of non-bacterial infections of the central nervous system is being investigated. The relative importance of diverse agents, especially the enteroviruses and arboviruses, as causes of aseptic meningitis, paralytic disease, and encephalitis will be assessed.

Rickettsial Diseases in Thailand.

SMRL, recognizing the importance of rickettsial disease in an evolving nation faced with possible military operations, has engaged in a project to define the problems of rickettsial disease in Thailand. The investigators use advanced techniques to isolate rickettsial agents from infected human beings, rodent reservoirs and arthropod vectors. The technique of immunofluorescence is used to provide reliable serological diagnosis of scrub typhus in cases

where actual isolation of the agent is impossible for one reason or another.

The project has produced ample evidence to show that scrub and murine typhus are ubiquitous in Thailand. In some areas of the north and northeast as many as 20% of patients hospitalized with pyrexia of unknown origin were found to have evidence of recent rickettsial infection. Vector mites and rodent reservoirs of scrub typhus are present throughout Thailand and present a serious threat especially in the northeast.

BACTERIAL AND MYCOTIC STUDIES

Bacterial Meningitis

In late 1967 there were a number of fatal cases of bacterial meningitis in children at Children's Hospital, Bangkok, Thailand. Physicians indicated that clinical courses and autopsy findings suggested bacterial etiology but the causal agent(s) were unknown. A study was started to ascertain the etiology of these infections, determine the antimicrobial sensitivities of the causal agents and to compare 3 antimicrobial regimens for the treatment of patients. Results to date indicate the causal agent is usually Diplococcus pneumoniae or Haemophilus influenzae. While all isolates of D. pneumoniae were sensitive in vitro to antibiotics in each regimen the mortality rate was 75%. Presumably this was because the children were seriously ill when first brought to the hospital.

Diarrheal Diseases

Several related studies of diarrheal diseases are in progress, including the continuing survey of stools from Thai & American patients with acute diarrhea to determine the types, frequencies of occurrence, antibiotic sensitivities, and distribution of pathogenic Enterobacteriaceae and vibrios. Shigellae are the enteropathogens isolated most frequently from Americans while Salmonellae, are isolated most frequently from Thais.

Other studies include microdetermination of Shigellae and Salmonellae agglutinins in human sera obtained from selected populations and a continuing in vitro evaluation of antimicrobials for effectiveness against diarrheal agents. The latter is particularly important in a locale where more than 10% of the indigenous population harbor enteric bacterial pathogens and antimicrobials are available without prescription. An example of changing patterns is the finding that in 1963 oxytetracycline was the antimicrobial

most effective against diarrheal agents whereas in 1967 it was one of the least effective.

Closely related to the above is a study of quantitative changes of intestinal and fecal bacterial flora of patients with acute diarrhea. Specimens include fluids aspirated from different levels of the intestine as well as stools. It was found that although there are great variations in the numbers of bacteria in most patients, coliforms were usually the predominant aerobes and gram negative obligately anaerobic bacilli were the predominant anaerobes.

Studies on cholera are directed toward an understanding of the mechanism by which cholera vibrios cause the voluminous diarrhea and toward developing more rational and effective methods of treatment and prevention of cholera. Extensive studies have been carried out on a cholera toxin factor, designated "Cholera toxin," which is elaborated by cholera vibrios during growth in the test tube. Minute amounts of "Cholera toxin" cause cholera experimentally in animals and, as an antigen, it elicits the production of antibodies which neutralize and precipitate it. Experiments in adult rabbits have demonstrated that parenteral injection of "Cholera toxin" gives rise to intestinal immunity to "Cholera toxin" and to massive live vibrio challenge.

In an effort to find an ideal antimicrobial for use in treatment and prophylaxis of cholera, in vitro evaluation of hydroxyquinoline preparations indicated they are effective vibriocides. Clinical trials conducted in a small number of cholera patients infected by the El Tor biotype indicated that oral iodohydroxyquinoline reduced the duration of vibrio excretion of patients, thus decreasing the hospital quarantine period.

Research carried out by investigators of the SEATO Clinical Research Center included clinical studies of intestinal immunoglobulins found in human small intestinal fluid and studies of human intestinal malabsorption syndromes. Immunoelectrophoresis procedures indicated that intestinal juices obtained from normal human Thai

volunteers contained predominately IgA, very infrequently IgG and IgM, and an unidentified substance of greatly variable electrophoretic mobility which reacted with normal goat serum and all goat antisera. Effects of tropical climates on the normal American intestine were studied in a group of Peace Corps Volunteers and a group of U.S. servicemen. These individuals, normal on arrival as regards gastrointestinal structure and function, developed a variety of abnormalities, for example, xylose malabsorption, Vitamin B₁₂ malabsorption, a tendency to absorb less lactose and decreased mucosal disaccharidase values. Jejunal biopsy specimens showed that most individuals developed changes including non-specific abnormalities and/or acute inflammatory changes, though none complained of persistent diarrhea, abdominal cramps or steatorrhea, nor was there evidence on physical examination to suggest malabsorption.

Melioidosis

Melioidosis is a polymorphic disease of man and animals caused by Pseudomonas pseudomallei, a bacterium virtually restricted to Southeast Asia. It is a relatively rare disease which the textbooks consider to be highly fatal. In neighboring Malaysia and Vietnam, Ps. pseudomallei has been found to be widely distributed in soil and water. When this SEATO study was initiated in 1965 there was essentially no information about the presence of the organism in Thailand or its importance as a disease agent. The organism has now been found to be widely distributed in soil and water in the South of Thailand and in a few provinces in the North Central and Eastern Regions. A highly sensitive and specific serological test has been developed at SEATO lab and serological surveys involving thousands of sera have demonstrated that a substantial proportion of Thai people living in areas where the Ps. pseudomallei has been isolated have antibody against this organism whereas in other areas the people do not have this antibody. Thus, it appears that Ps. pseudomallei is a more benign organism than was formerly thought and might be regarded primarily as a saprophytic oppor-

tunist. However its widespread presence makes it necessary to consider melioidosis in the differential diagnosis of infectious diseases in Thailand.

Mycotic Diseases

To gain information on the prevalence and distribution of mycoses of importance in this area of the world, histoplasmin sensitivity tests were conducted in adults in various parts of the Thailand with the following results: In the North, Northeast, and Northcentral areas the rate of positive reactors was approximate 5 percent; in the Central provinces 18 per cent; and in the Southern peninsula 25 per cent.

The ecologic studies of pathogenic fungi in Thailand have centered around the study of soil and attempts to detect naturally acquired mycoses among the rodent population. Results have been discouraging except for the recovery of Cryptococcus neoformans from pigeon habitats. Clinical specimens were also collected and cultures made at the dermatology clinics of three Bangkok Hospitals. The most striking finding was the role Candida albicans plays in the role of skin diseases. Otherwise the dominant pathogens are the same species commonly encountered in the U.S. Exceptions include a few cases of Tinea imbricata which is geographically restricted to this area of the world, and morphological differences noted in strains of Trichophyton rubrum and Microsporum canis.

Plague

Studies in Vietnam on the ecology of plague reservoirs and vectors at various locations have yielded data useful for plague control program planning. Studies on Vietnamese nationals hospitalized with plague, and on their household contacts, have provided new information on clinical features of the disease.

Studies in Thailand, which has been free of plague since 1952, are directed to assessment of potential reservoirs and vectors, and

to a search for possible residual sylvatic foci. These studies may be of practical value in the event of introduction of plague into receptive areas of Thailand.

Upper Respiratory Infections

The objective of this study is to evaluate the efficacy of antimicrobials now in use for prophylaxis of upper respiratory infections in Thai children and to determine the effects of these antimicrobials on the flora of the upper respiratory tract. Studies to date show that the bacterial pathogens isolated most frequently are Diplococcus pneumoniae, coagulase positive Staphylococcus aureus and Haemophilus influenzae. Viruses isolated most frequently were cytomegalovirus and enterovirus. Evaluation of antimicrobial prophylaxis must await completion of the double blind study when the formulations of the treatment regimens are disclosed.

Venereal Diseases

SMRL studies of gonorrheal infections in Thailand were initiated following reports that cases of clinical urethritis—presumably gonorrhea—were not responding to prescribed doses of penicillin. Aspects studied include evaluation of diagnostic techniques, antibiotic sensitivity determinations of isolates of Neisseria gonorrhoeae, evaluation of chemotherapeutic regimens and detailed studies of the urethral flora of patients who fail to respond to antibiotic therapy.

The value of a rapid, reliable presumptive test in areas where bacteriological support is not readily available is self evident. Evaluation of 2 such procedures—the fluorescent antibody technique and the cytochrome oxidase test—indicated they are unreliable for rapid diagnosis of gonorrhea in females. However a new commercial culture medium supplemented with a chemically defined enrichment and made selective by adding antimicrobials was found to be superior to previously used media for isolation of gonococci from females. Sensitivity studies have shown that all strains of

N. gonorrhoeae isolated since this study was initiated in 1964 were sensitive to readily achievable blood levels of penicillin or tetracycline. The urethral flora of patients who fail to respond to antibiotic therapy usually includes penicillin-resistant gram positive cocci or gram negative rods.

No research studies on syphilis are in progress except serology (VDRL) testing of sera. Less than 10% of 677 sera from Thai nationals and less than 2% of 542 sera from U.S. servicemen were positive during the last year.

ENTOMOLOGIC STUDIES

1. ECTOPARASITES

The objective of SEATO Medical Laboratory studies on ectoparasites is to assemble information on the host-parasite relationships of the various groups of ectoparasites in Thailand, their geographic distribution, abundance, and other facts on their bionomics. These studies are carried out in conjunction with and in support of the studies on rickettsial diseases, plague and arboviruses. Ectoparasites collected from mammals, birds, and reptiles in Thailand are identified either by SEATO personnel or by outside authorities, and descriptions of new species are prepared for publication together with keys to the groups of medical importance. The eventual aim of these studies is the production of a catalogue of all of the important ectoparasites in Thailand, together with pertinent information on their distribution and habits, for use in future ectoparasiteborne disease studies.

2. MOSQUITOES

SEATO Medical Research Laboratory studies on mosquitoes are concerned with the distribution and behavior of the vectors of such mosquito-borne diseases of military importance as malaria, dengue, and Japanese encephalitis. The identification, description, and cataloguing of the mosquitoes of Thailand with the object of developing keys to the identification of the species of medical importance is another major goal of these studies. Publications dealing with the distribution and habitats of these species have been and are being prepared. Many of the mosquitoes collected during these studies have been carefully organized to form the nucleus of a future national reference collection for use by Thai and foreign scientists. Laboratory colonies of mosquitoes such as Anopheles balabacensis, An. stephensi, An. maculatus, Aedes aegypti, Aedes albopictus, Armigeres subalbatus, and Culex quinquefasciatus have been established for the purpose of research on the transmission

of many of the above diseases and for the evaluation of insecticides and chemical repellents for use in control of these insects. Studies on the insecticide tolerance of vector species of mosquitoes in Thailand have been undertaken in an effort to evaluate the effectiveness of chemicals presently used in malaria and dengue control programs. Cooperative studies with Thai and American government agencies are carried out to test newer and more effective materials for the control of mosquitoes. A continuing surveillance of the insecticide tolerance of mosquitoes from various parts of Thailand is maintained by the Department of Medical Entomology in cooperation with the World Health Organization. Field investigations on the vectors of malaria and arbovirus diseases are being carried out in selected areas where the effects of mosquito density, host preferences, longevity, and flight ranges upon the incidence of these diseases are measured. Since Thailand has such a wide variety of terrain and vegetation, mosquito-borne disease situations differ in each region and specific measures of control must be developed for each type of association.

PARASITIC DISEASES

Eosinophilic Meningitis

Eosinophilic meningitis is an important disease syndrome of the central nervous system in Thailand. Investigations in this laboratory have divided the syndrome, based upon symptomology, into two entities, namely "typical" eosinophilic meningitis and eosinophilic myeloencephalitis. The major symptomological distinctions are that headache is a constant complaint in typical eosinophilic meningitis but not in myeloencephalitis and limb paralysis is not found in typical eosinophilic meningitis while it is common in myeloencephalitis.

Evidence acquired implicates the rat lung worm, Angiostrongylus cantonensis, as an important causative agent in typical eosinophilic meningitis. This parasite may be acquired by consumption of raw snails. Investigations have also shown that many common snails and slugs are capable of serving as intermediate hosts. It has also been shown that it may be possible to acquire this parasite by consumption of water inhabited by larvae of A. cantonensis and that ordinary chemical treatment of water may not be sufficient to destroy these larvae.

Recent research has implicated Gnathostoma spinigerum as a causative agent of eosinophilic myeloencephalitis. This parasite was isolated from the brain tissue of two fatal cases in Thai nationals. The intermediate hosts and route of infection remain to be determined.

Filariasis.

This laboratory is conducting investigations into the epidemiology of human and animal filariasis. In some areas of Southern Thailand, almost 10% of the human population had evidence of being infected with Brugia malayi. Periodicity and specific transmission vectors remain to be investigated.

Brugia tupaia and three, as yet, unclassified types of microfilaria have been found in various animals trapped in Thailand. B. tupaia has been found exclusively in the tree shrew, Tupaia glis, while the others have been found in rats (Rattus rattus and Rattus rajah) and in the ground squirrel, Menetes berdmorei. Laboratory investigations have shown that Aedes togoi and Armigeres subalbatus may be involved in the transmission of B. tupaia.

Gnathostomiasis.

Human and animal gnathostomiasis caused by Gnathostoma species are endemic to Thailand and the incidence appears to be increasing. Human cases of gnathostomiasis that have been recognized are due only to one member of the species, namely, G. spinigerum while G. doloresi and G. hispidum infections in animals (particularly pigs) have been noted. Extensive investigations into the taxonomic classification, life cycle, intermediate and primary hosts, and host pathophysiology of the various members of Gnathostoma species are being conducted.

Intestinal Parasites.

A survey of the helminth infection of dogs in the city of Bangkok has been undertaken because of recent reports that many of the parasites are potentially transmissible to man. A large number of the dogs examined have been found to be infected with one or more species of helminths. Of those found at least the following species can be considered as infective to man: Ancylostoma sp., Trichuris vulpis, Toxocara canis, Gnathostoma spinigerum, Spirocerca sp., Dipylidium caninum, Opisthorchis viverrini, Diphyllobothrium sp., and Fasciola/Fasciolopsis.

The effects of the development of the Kingdom of Thailand over the last 15 years has been pointed out in a recent survey of the incidence of Fasciolopsis buski. As a result of improved

drainage and flood control the rates of F. buski infection have been greatly reduced. Areas which are flooded for a major portion of the year still show high infection rates. Laboratory studies are currently in progress in which the life cycle and the delineation of intermediate hosts are investigated. These studies have indicated that areas which are exposed to tidal waters would not be areas in which F. buski would survive as the development of the parasite was arrested in salt water.

Clinical examination, evaluation of growth and development, hematologic studies and screening tests for malabsorption syndrome in patients with F. buski infection did not reveal significant differences between them and controls. As a result of this clinical study it was concluded that F. buski infection probably is not directly responsible for overt clinical disease in Thailand.

Malaria.

Malaria studies comprise a large portion of the research work done in this institution. Studies involve the response of humans to disease, means of prophylaxis and treatment, bionomics and population dynamics of the vectors, development of animal hosts to human malaria, definition of the response of animals to human malaria and their suitability as experimental hosts, immunologic responses of animals to animal malaria, and metabolism and respiration of the parasite.

Mosquitoes are studied both by means of laboratory colonies and wild caught specimens. Better understanding of host preference, biting habits, flight patterns, environmental preferences, and similar data are sought. Long term studies of the effect of the various seasonal variations on vector populations are currently underway.

Studies of malaria in humans have generally centered on the effects of the infection on the central nervous, hepatic and renal systems.

A comparative study of host-pathophysiology using the simian malaras, Plasmodium coatneyi, P. inui, and a taxonomically unclassified malaria of the gibbon are being conducted. The results obtained indicate that P. coatneyi produces, in the rhesus monkey, a clinical course of disease similar to that caused in humans by P. falciparum and it has been suggested as a model so that a better understanding of the disease producing mechanism of P. falciparum can be obtained.

Immunologic studies have been undertaken using simian and rodent malaras. Partial protection against the rodent malaria, P. berghei, has been obtained using specially prepared antigens.

Investigations into the basic metabolic processes of host cell-free preparations of P. berghei have shown that certain metabolic processes previously thought not to occur in the parasite, are actually present. By investigating metabolism in depth and comparing it to that of the host erythrocyte a better understanding of the host-cell specificity and metabolic needs of the parasite is sought.

NEUROPSYCHIATRY

The goal of neuropsychiatry is to study how neural, cultural, social, and personality factors influence human behavior. Within this context, work concerning transcultural communication, advisor-counterpart relationships, adaptational problems of U.S. families abroad, and studies of socio-cultural organization of communities are being carried out by a staff of psychiatrists, associated contract social anthropologists, and collaborating Thai psychiatrists.

The studies of transcultural communication and advisor-counterpart relationships concern factors influencing information exchange and performance in a situation where representatives of different cultures are required to collaborate in the accomplishment of a task. A study, focused on the relationship between transcultural communication and medical student behavior, was conducted at the Faculty of Medicine of Suan Dok Hospital, Chiang Mai, where U.S. medical educators are cooperating with the Thai faculty in the development of a recently founded medical school. The results of that study are currently being analyzed. In addition, a Thai and American psychiatrist are jointly examining the relationships between U.S. advisor and Thai counterparts in the military. The influence of such factors as organization structure, value commitments, individual adaptation, language skills, and interpretation of task definition upon the behavior of the advisor and counterpart is being evaluated.

A study concerning the disturbances of thinking in organic brain syndromes is in progress. This work has the goal of developing reliable clinical techniques and tests to assess the psychological manifestations of cerebral dysfunction due to drugs, neurosurgical disease, and infectious disease. By examining how patients and their family respond to the stress of illness, information is being acquired about the incorporation of the basic symbols of Thai culture into thought patterns of individuals.

The social anthropologists associated with the Department of Neuropsychiatry are performing research into the social and cultural organization of human behavior in various ethnic groups. These studies are particularly interested in the relative part played by traditional and modern health practices in the context of the community structure. Attention is being given to what people do to keep well, how they recognize that they are ill, what they do about illness, and what their general ideas about illness are. In addition, data about kinship ties, institutional structure, religion and rituals, and economic organization of the communities are being collected in order to provide basic understanding of the ethnographic background of each area under study.

A study has been initiated to examine the articulation and adaptation of U.S. citizens to the environment in a town in North Thailand. It will examine how these American families perceive and participate in the culture of that town, with emphasis on their use of one part of that culture, the medical system. This study is designed to provide insight into the relations between the reported intra-family interactions and the family's pattern of exchange with its human environment. An understanding of this will be useful to military or civilian administrators of "overseas" agencies. The information about illness, its treatment, and the use of the medical care system will provide information useful in the planning of a medical support program.

The Department of Neuropsychiatry is cooperating with the Thai Consultant to the Chief of the Clinical Research Center in an extensive program of social psychiatric research. The main thrust of this work will be to develop a program for facilitating the reintegration of the chronically ill person afflicted with schizophrenia back into the family in the non-urban community by supporting appropriate institutional behaviors that facilitate favorable community attitudes. This study will provide basic data about the response of the Thai community to the chronically ill schizophrenic member. Such data will be of value in the development

of a community health program relevant to the needs of the chronically ill and in increasing our understanding of how illness and its cure may be influenced by and influence a wider range of human transactions in the community.

An experimental course in programmed Thai has been brought to Thailand for evaluation and further development. This program employs the principle of successive approximation and is presented by means of a self-instructional, automated, audio-visual device. Data obtained in the course of this experiment will be used to assess the value of the program as an effective method of teaching the Thai language; to modify the techniques and content of the program; to evaluate basic language aptitude, educational experience, and environmental contingencies as potential influences upon performance in the program and retention of learned material thereafter.

The research effort in neurology is directed toward the investigation of nervous system function in acute infectious diseases. Our immediate goals are to define better the role of hypoxia in the pathogenesis of cerebral symptoms in malaria and to examine a few of the ways the brain responds to and copes with the stress of a systemic infection.

Experiments designed to answer these questions now center mainly around cerebral hemodynamic and metabolic measurements in normal subjects, volunteers with induced fevers, and patients with malaria. Nitrous oxide, a diffusible tracer, is being used to measure mean cerebral blood flow. Data is now being collected on cerebral blood flow, cerebral vascular resistance, oxygen consumption, oxygen content and carbon dioxide, pH $p\text{CO}_2$, glucose, lactate and pyruvate differences in normal Thais.

ANIMAL STUDIES

Ecology of the Gibbon

The project on the ecology of the gibbon has as its main purpose the study of caged and feral gibbons with a view ultimately to develop an economically feasible procedure for producing infants for scientific and conservation purposes.

At the Phrabuddhabat laboratories, nine pairs of gibbons were maintained in outdoor cages to determine what level of infant production is possible under good laboratory conditions. All of these pairs were healthy and socially compatible and seven were seen to copulate. During the past year one female has given birth to a female infant who was still doing well with her at the age of 3 months. At the time of this writing two other females are pregnant.

Ko Klet Kaeo, an island in the Gulf of Siam has been developed as a research station for ecological studies of primates of Thailand. The flora and fauna of the island have been surveyed. Thirteen of 19 gibbons introduced onto the island have survived and copulation by 3 of the pairs has been observed. No pregnancies are apparent yet. Gibbon home ranges exceed 40 acres in natural habitats but are no larger than 8 acres on the island facility where cover is thick and where food and water are freely available. In such a situation social factors apparently are the main determinants of territory size and shifts. In related studies it was determined that gibbons live and reproduce in 15-acre isolated forest patches and preliminary studies have shown that radio tracking of gibbons in the forest is feasible.

Laboratory Animals

The use of non-human biological hosts is essential to medical research. It is also essential that parameters of these host systems be defined and that variability in the animal population be reduced to the minimum to insure consistent experimental results.

Studies in laboratory animals have been in two major areas. The first of these has been designed to develop and improve techniques in the production of the conventional laboratory animals such as rats, mice, guinea pigs, and hamsters under the environmental conditions which are present in Thailand and to insure a greater degree of genetic and physiologic uniformity in these animals. The second major area of study has been in the selection and development of previously undefined animals for laboratory use. The white-handed gibbon (Hylobates lar) and the tree shrew (Tupaia glis) have been investigated for potential colonization and laboratory suitability.

Vertebrate Ecology

The objective of this study is to study the rodents of Thailand and develop a taxonomic system which can provide a basis for ecologic studies of zoonoses involving rodents. Twenty-six of the 27 species of rats and mice characterized are native to Thailand. The Muridae of Thailand comprise the following groups:

<u>Bandicota</u> , Bandicoots	2 species
<u>Rattus</u> , Rats	17 species, 5 of which are commensal with man.
<u>Mus</u> , Mice	4 species
<u>Arboreal rats and mice</u>	4 species with hands and feet specialized for climbing trees.

Wobbler Syndrome in Horses

A condition clinically similar to cerebrospinal nematodiasis or "Wobblers" has been observed for several years in the horses at the Royal Thai Army Breeding Farm at Kanchanaburi, Thailand. Investigations of this condition included clinical observations, hematologic studies, cerebrospinal fluid studies and necropsies.

Thirty-seven of 140 horses were found to have various stages of the wobbler syndrome. Affected horses ranged from six months

to twelve years in age. The primary manifestations of the syndrome were an incoordinated gait, particularly in the rear legs, and staggering and falling when backing.

Microfilariae were found in the peripheral blood of two affected horses. In a previous survey done in March, 1967, 18 of 21 horses had microfilariae. Necropsy of characteristic cases revealed grossly visible focal areas of yellowish gelatinous softening in the brain. They were found in and around the internal capsule, putamen, thalamus, and in the central white matter of the cerebral cortex. Microscopically, the areas were focal cavitations surrounded by malacia, demyelination, and loss of nervous tissue components in the area. Blood vessels and accompanying connective tissue formed a lacy spider web pattern throughout the area of malacia. Pigment laden "Gitter cells" were numerous in the area. No parasites were found although calcified and small fragments of foreign material were occasionally seen in serial sections of the lesions. The etiology of this condition remains to be determined.

PART III

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