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**SEATO**

**MEDICAL RESEARCH PROGRAM**

**BANGKOK, THAILAND**

## PREFACES

### 1.

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 over-whelming 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 is 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.



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2.

The debilitating effects of disease may be manifest for lifetime. Disease from infection and malnutrition can begin at birth - for example, syphilis, tuberculosis and diarrheal disease. The manifestation of severe anemia due to parasites during the first five years of life can developmentally influence one's ability in adulthood. It is wasteful and inefficient to have to "build up" recruits or civilian forces before effective civilian and military training can take place. With the joint medical efforts and researches directed towards the objectives of the SEATO Medical Research Program, there will be improvement of health and medical care through education, training, and research. The scientific progress accomplished in medical research and training in cooperation with Thailand and other SEATO nations is for the benefit of all.

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## ANTIMICROBIALS

These studies concern the antibiotic sensitivities of bacterial agents which are of present and potential importance. These studies have involved the bacterial flora found in association with diarrheal disease, respiratory disease, urinary tract infections and infections of both traumatic and post-operative wounds. Studies of the latter are continuing in collaboration with the Police Hospital in Bangkok. A study of the effectiveness of topical antibiotics in the prophylaxis and therapy of traumatic injuries sustained in combat has recently been completed and the data are being analyzed.

The common bacterial pathogens associated with diarrhea in Thailand are usually resistant to antibiotics other than neomycin or tetracycline.

## ARBOVIRUSES

Present programs include epidemiologic surveillance of hemorrhagic fever in Bangkok and attempts to document the spread to previously unaffected areas of Thailand. The pathogenesis of hemorrhagic fever due to dengue infection is not clear at present. The basic cause of the shock phase is unknown and studies are in progress to determine the nature of the immunologic response and its relationship to the vascular abnormalities in hemorrhagic fever cases by collecting serial serum specimens during the course of the illness and using ultracentrifugation, gel chromatography and immunoelectrophoresis to separate immunoglobulin fractions which are then tested for antibody by hemagglutination inhibition and neutralization tests. Serial studies on complement levels and interferon levels are also being done.

The plaque neutralization test is being developed and standardized for studies on the nature and specificity of dengue antibodies in man and experimental animals. Studies on monkeys infected with dengue viruses indicate that both 19S and 7S antibodies are produced and tests on the relative specificity of these antibody in man following dengue infection is highly specific for the infecting type following the first dengue infection, after infection with a 2nd or 3rd type of dengue virus the antibody response is very broad and cross-reactive. Fractionation of human serum is being done to determine the relative specificity of the 19S and 7S fractions following the first dengue infection, after infection with a 2nd or 3rd type of dengue virus the antibody response is very broad and cross-reactive. Fractionation of human serum is being done to determine the relative specificity of the 19S and 7S fractions following both primary and secondary dengue infections.

The methods available for identifying and typing of dengue viruses are unsatisfactory. It has been recently found that highly specific antiserum can be made in monkeys if they have not had previous group B arborivirus infections. Using monkey serum and plaque reduction neutralization tests the antigenic relationships of the dengue viruses are being studied. Strains of dengue isolated from hemorrhagic fever cases are being cloned by plaque methods and compared with reference dengue strains.

Japanese encephalitis virus has been shown to produce human disease in Thailand. Outbreaks of encephalitis due to this agent were documented in Pisanuloke in 1964, and Chiangmai in 1965. Sporadic cases from Korat and Chachongsao have been proven, and one fatal case occurred in an American soldier.

Diagnostic studies on cases of central nervous system disease from hospitals in Bangkok, Korat, Chiangmai and Phrabuddhabat are being done to determine the relative importance of arboviruses as causative agents of encephalitis and aseptic meningitis. Three cases of CNS disease, one fatal, have been shown to be due to Chikungunya virus.

Studies on the basic ecology of JE and Chikungunya virus in nature are in progress. Birds and large and small mammals including bats are being studied to determine their importance as reservoir or amplifying hosts. Parallel entomologic studies on mosquito vectors are also being done. The major study area is at Bang Phra where 18 strains of JE virus have been isolated from mosquitoes in the past 3 years.

## BLADDER STONE

Bladder stone is an acute and chronic disease occurring in many countries, including Egypt, South India, Burma, Pakistan, Indonesia, and Thailand. It is the most common surgical problem among over one-half of the population of Thailand and occurs predominantly among rural inhabitants of the North and Northeast. Previous epidemiological studies revealed that prevalence of positive stone histories was 12, 19, 23, and 7 per 1000 persons in Ubol, Khonkaen, Chiangmai and Korat respectively. There is a marked disease activity during the first 5 years of life.

Studies of the dietary habits in village as compared to the city inhabitants during the hot, raining and cool seasons of 1963 revealed that vitamin A intake among villagers (724, 861, and 1133 I.U./day) was about half that of city inhabitants (1720, 1810, and 2528 I.U./day). Protein intake, especially animal protein, was lower in Nong Kohn village. There were striking differences in the age of introduction of solid food to the infants. Fifty-seven percent of village infants had their diet supplemented with baked and chewed glutinous rice during the first week of life as opposed to 2 percent among infants in the city. Subsequent studies in the Central North and Northeast Thailand revealed a highly significant correlation existed between early rice feeding and stone prevalence in Korat Province (the most westerly of the 16 provinces in the Northeast).

Urologic studies, including 24-hour and casual specimens, revealed that volume of 24-hour urine excretion in subjects living in Nong Kohn village (endemic area) was about half that of subjects living in Ubol city, during the hot, dry weather (April 1963). The same group of villagers excreted about half as much during the hot season as compared to the rainy and cool seasons.

Selected urinary metabolites study in children from 2 to 10 years old including Ca, P, Mg, creatinine, uric acid, and oxalate, revealed a higher urinary calcium excretion in villagers as compared to the city inhabitants in all three seasons. There are no other significant differences in metabolites excreted by these two groups. Study of the urinary amino acids, sulfur and mucosubstances in 24-hour specimens collected from infants living in villages and the city is in progress.

## CARDIAC DISEASE

Studies in the Clinical Research Center have defined the normal physical and electrocardiographic criteria for the child and young adult population of Thailand. These criteria differ significantly in some respects from those of occidental populations, perhaps as the result of the low incidence of coronary artery disease and hypertension. This study also revealed that over three percent of the population in this age group may be affected by congenital malformations or rheumatic damage to the heart.

Subsequent studies have attempted to define the relative prevalence of each type of congenital malformation, and here again, a significant difference from western experience has been shown. Coarctation, is rare in this country compared to Western countries. Continuing studies, carried out in the cardiac catheterization laboratory of the Pra Mongkut Klao Hospital, are aimed at defining the metabolism of the heart in various disease states, including the changes produced by drugs commonly used in treatment of cardiac disorders. Studies of the treatment of shock in overwhelming infections will be carried out at the Siriraj Hospital.

## CHOLERA

The SEATO Medical Research Program on Cholera is a basic scientific research study directed primarily toward an understanding of the mechanism by which cholera vibrios cause the voluminous diarrhea which characterizes this disease. With an understanding of the actual pathogenetic mechanism it should be possible to develop more rational and effective methods of treatment and prevention. SEATO Medical Research Laboratory Investigators have described, isolated and purified, for the first time, an extremely active choleraogenic factor, which they call "cholera toxin", which is elaborated by cholera vibrios during growth in the test tube and which causes cholera experimentally in animals and in human volunteers. Less than four millionths of a gram of cholera toxin suffices to cause experimental cholera in infant rabbits, the only laboratory animal which reproduces the disease as it occurs in man. Cholera toxin is antigenic and elicits the production of antibodies which neutralize it and precipitate it. However, these antibodies are not protective when administered systemically in infant rabbits. Thus, it appears that antibody to cholera toxin may have to be stimulated locally in the intestinal tract to be useful in protecting against the disease in man. Current efforts, directed to increasing our understanding of how cholera toxin actually causes cholera, have led to the operational concept that cholera toxin alters the permeability of the vessels in the microcirculatory system of the intestinal villi.

In addition, SEATO lab is always prepared to assist local health authorities when the threat of cholera arises with round-the-clock bacteriological support because it is recognized that rapid diagnosis and isolation of patients and carriers can prevent serious outbreaks of this dreaded disease.

## DIARRHEAL DISEASES

There are several related but distinct studies of diarrheal disease in progress. One is a continuing survey of stools from patients with acute diarrhea. Its objectives are to determine the types, frequencies of occurrence, and distribution of salmonellae and shigellae in the stools of Thai and American patients with acute diarrhea and to determine the incidence of Enterobacteriaceae and their relationships to this disease. This study is now being expanded to include parasitological examinations of stools from Thais and Americans with or without acute diarrhea in all areas of Thailand where American troops are stationed.

Closely related to the above is a study of quantitative changes in fecal bacterial flora of patients with acute diarrhea. Specimens include fluids aspirated from different levels of the intestine as well as stool. In addition the influence of antimicrobial agents administered therapeutically to diarrhea patients or experimentally to controls are being determined in terms of bacterial flora. Investigations in other parts of Southeast Asia have suggested that there are distinctive structural and functional abnormalities of the small bowel peculiar to this part of the world. Clinical studies of absorptive function are being carried out to characterize these abnormalities and to discover causative factors such as vitamin or other dietary deficiencies, intestinal infections, or parasitic infestations. It is anticipated the parasitological studies and quantitative bacteriological studies will supplement information provided by these studies of the small bowel.

An epidemiological study is nearing completion in Chiangmai, Thailand. Its objective is the determination of factors which influence the epidemiology and endemicity of enteric infections in that area. This problem has been subdivided into several simultaneous studies of factors likely to be important in the spread of enteric infections. Some of these are bacteriological analyses of drinking water, flies, cockroaches, and foods from various sources; survival of known pathogens in water and on foods usually eaten raw; a year long survey of school children to discover frequency of carriage of parasites; and serological surveys of residents to determine prior exposure to enteric pathogens. An attempt will be made to relate the above to clinical records at Chiangmai hospitals.

## ECTOPARASITES

The objective of SEATO Medical Research 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 disease and leptospirosis. 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 ectoparasite-borne disease studies.

## EOSINOPHILIC MENINGOENCEPHALITIS

Eosinophilic meningoencephalitis is a disease which is thought to be produced by the invasion of the central nervous system by the larval form of parasites. In Thailand, evidence shows that most cases are associated with infection by the lung worm Angiostrongylus cantonensis. A typical clinical syndrome is produced in man. In the study of the spinal fluid in such a case a high percentage of eosinophils are found. A paper was given by Major Sompone Punyagupta, MC, Royal Thai Army on this disease at the First Medical Conference on Parasitic Disease sponsored by the US Army Component, SEATO Medical Research Laboratory, December 1964 in which he presented the material on nine cases occurring in Thailand. Following this paper several projects were developed in collaboration with Major Sompone Punyagupta, Royal Thai Army Hospital to further study this disease. These studies deal with the human epidemiology, clinical manifestations, and pathology, and the natural mammalian infection. Coordination of these studies has been made with Dr. Leon Rosen of the Pacific Research Laboratory in Hawaii. Dr. Rosen was among the first to report human disease from eosinophilic meningoencephalitis in the South Pacific area. As of 30 September 1965, over 77 human cases have been clinically diagnosed in Thai people, and 7 cases have been found at autopsy. More recently it has been shown that transverse myelitis can be a prominent symptom and also that the gnathostoma parasite may be incriminated as another cause of the disease.

## GNATHOSTOMIASIS

Human cases of gnathostomiasis have been recognized in Thailand as due to Gnathostonia spinigerum. The prevalence of infection is not known. Dogs, cats, tigers and leopards have been shown to be natural hosts and can function as reservoir hosts.

Present studies aim to determine the prevalence of human and animal cases. Case reports are collected from 92 hospitals in various parts of the country and from local practitioners in areas which are considered to have a high degree of prevalence. Approximately 800 suspected cases are identified annually. Attempts to develop a sensitive skin test are planned.

Studies of the significance of animals as reservoir hosts are done by means of examining stools and gastrointestinal tracts for adult worms. About 9% of domestic cats and 1% of dogs have been found to be positive.

Additional studies of natural or potential second intermediate hosts are being done. By feeding animals with second and third stage larval, it has been possible to identify 15 more potential intermediate hosts in addition to the 21 already known. These are spread through five classes of animals; Reptilia, Pisces, Amphibia, Aves, and Mammalia. Ducks and chickens have been shown to have very high infectious rates.

## GONORRHEA

Studies of gonorrheal infections in Thailand were initiated in Thailand following reports that cases of clinical urethritis - presumably gonorrhea - were not responding to prescribed doses of penicillin. Phases of the study already completed are evaluation of culturing techniques, antibiotic sensitivity determinations of isolates of Neisseria gonorrhoeae, measurement of antibiotic concentrations in the blood of patients being treated, evaluation of chemotherapeutic regimens and detailed studies of the urethral flora of patients who fail to respond to antibiotic therapy.

Direct streaking of swabs onto Thayer-Martin medium followed by incubation at 37 C in an atmosphere of 3 to 5 percent CO<sub>2</sub> for 24 hours prior to transport to Bangkok proved to be a satisfactory procedure for field studies. All of more than 200 isolates of N. gonorrhoeae tested were sensitive to 1.2 units/ml or less of penicillin and to 2.4 mcg/ml or less of tetracycline. The average resistance of strains isolated in the last two months is about one-third higher than isolates obtained the first three months of 1965.

Measurement of penicillin blood levels of Thai female patients at venereal disease clinics following a single prophylactic injection of penicillin revealed that the dosage used provided blood levels exceeding the average minimal inhibitory concentration of these strains for no more than eight hours and that this procedure was probably providing an environment for the emergence of resistance strains. This procedure has been revised by Thai medical officials so that adequate dosage are given.

Antibiotic regimens were evaluated in institutionalized patients in terms of cultural findings and blood levels achieved. It was shown that clinical cures and adequate blood levels of penicillin and tetracycline could be achieved with penicillin and tetracycline. However the concept of maintaining blood levels in persons at high risk by weekly injections of benzathine penicillin was shown to be inadvisable.

Currently studies are being carried out on American males to determine the bacterial flora of urethral exudates, the sensitivities of all isolates to penicillin and tetracycline and, particularly, to study therapeutic failures. It has been found that most specimens contain two or more organisms and it is not unusual for the organism found concomitantly with N. gonorrhoeae to be resistant to penicillin and tetracycline. Occasional isolates of the Mimae-Herellae group have been made but not from patients judged to be therapeutic failures. Other organisms isolated frequently are coagulase positive staphylococci, coagulase negative staphylococci and diphtheroids.

## GROWTH AND DEVELOPMENT

To our knowledge, there has been very little information available regarding normal growth and development in Thais. Western standards have always been used as a reference for normal. Thailand is different from Western countries in many ways; for instance climate, dietary habits and culture. In general, Thais have less protein and calcium intake than Caucasians. Rice is the main staple food in Thai diet. It is important that this type of information be obtained so that valid observations on states of metabolic and nutritional abnormality may be made.

The first study along this line is a "Radiologic Study of the Development of Ossification Centers in Normal Thais". Work has just begun recently so no data are available yet.

## HEMATOLOGY

Hematology research has been in two major areas. The first of these was a study of anemia. During 1964, a survey team sampled various areas of the country in an attempt to ascertain the prevalence of anemia, the degree of anemia and to collect information on the types or causes of anemia. One thousand sixty-four subjects were studied from four areas of the country. A general physical examination was performed and blood drawn for hemoglobin, hematocrit, RBC morphology, malaria smear, serum Fe and TIBC, hemoglobin electrophoresis, and G-6-PD assay. The overall prevalence of anemia varied between 70% to 89% in different regions. The most common cause of anemia was iron deficiency. Although hookworm infestation was found to be common in the South and could well explain anemia there, this was not true of the other areas studied. An additional study in the Bangkok area is nearing completion at the present time in which an attempt is being made to assess dietary iron intake by analysis of stool iron. Approximately one third of the twenty-nine subjects studied show levels below the recommended intake. Two additional factors that may play a role in iron deficiency are malabsorption of iron as part of a generalized malabsorptive state or unavailability of the food iron. Studies are underway which may help clarify this in the future.

The second area of interest has been in RBC glucose-6-phosphate dehydrogenase (G-6-PD) deficiency. As part of the anemia survey, prevalence of this abnormality was also studied. The various tests to measure this abnormality were compared and data were accumulated on the effect of storage on enzyme activity. Present studies in this field measure physiologic abnormality in the absence of clinical manifestation, specifically, red blood cell survival and iron storage. In addition, enzyme purification preparatory to characterization is nearing completion. Incubation studies of the pentosephosphate pathway in cells which have no G-6-PD activity spectrophotometrically, have shown that this pathway is active, although reduced. Further studies are planned in an attempt to explain this phenomenon.

Future work will be based on the findings of present studies. In addition, SMRL will be giving partial support for a large scale study of population genetics of hemoglobin E, thalassemia and related genetic polymorphisms which will begin in the near future.

## LABORATORY ANIMALS

Much medical research entails the use of non-human biological hosts. Choice of such a host varies with the type and nature of the experimental design. This study has been designed to develop and improve techniques employed in large scale production of laboratory animals (mice, rats, guinea pigs and hamsters). Animals originating in a defined environment contribute markedly to the consistency of results in investigations. New, previously undefined animals such as the gibbon (hylobates lar lar) and the tree shrew (Tupaia glis) are being investigated for both colonization suitability and biological acceptability.

Animal production has markedly increased in the mouse, hamster and rat colonies. Due primarily to the changing of colony management techniques, the tree shrew (Tupaia glis) has been colonized and techniques for large scale production have been established. Parasitological, bacteriological, hematological and biochemical data have been compiled and will prove useful to interested investigators. The department is now involved in colonization of the gibbon (hylobates lar lar). Preliminary investigations will involve determination of suitable environments for reproduction. Since various techniques must be investigated, use of an island for free range as well as large cages will be investigated. Behavioral patterns are studied to determine adaptability of the species to these artificial environments. This species, following splenectomy, is a very suitable biological host for studies in malaria. This will enable investigators to study chemotherapy and immunology associated with this disease.

## LEPTOSPIROSIS

The leptospiral organism is responsible for producing disease often diagnosed as "fever of unknown origin" in the human. In collaboration with the Department of Livestock Development, Ministry of Agriculture the significance of wild and domestic animals as reservoir hosts and the role of water in paddy fields and klongs in the transmission of the disease is being investigated. The study consists of isolation of the organism either by inoculation of the water sample into weanling hamsters or by direct culture of rodent kidneys. Kidneys are cultured from the inoculated weanling hamsters dying between 4 and 21 days post inoculation. Rodent and suspected hamster kidney tissue is inoculated directly in Fletcher's media enriched with rabbit sera. The isolates obtained are typed by standard leptospiral serological methods. Serological prevalence of leptospiral agglutinins in domestic livestock and humans is also studied utilizing eighteen (18) serotype antigens. Data indicate that both the dog and rodent play a major role in transmission of the disease in urban areas. Field studies are currently underway to determine prevalence and vehicles of transmission in Southern Thailand.

## MALARIA

Malaria studies comprise a large portion of the research work done in this institution. Seven of the nine scientific departments are involved in one or more aspects of this disease. 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 suitability as experimental hosts, immunologic responses of animals to animal malaria.

Studies of malaria in humans have been both clinical and therapeutic. At Phra-buddhabat Hospital in the Province of Saraburi, clinical studies of cerebral malaria and hepatic malaria have been in progress since August 1965. These studies are conducted jointly with the hospital staff. Recently, several new studies involving varied therapeutic regimens for cerebral malaria and for uncomplicated malaria have been started.

Surveys of the prevalence of chloroquine resistant falciparum malaria have been done in several parts of Thailand. In some areas, 70% of the strains found did not respond to a full therapeutic course of chloroquine.

Mosquitoes are studied both by means of laboratory colonies and wild caught specimens. Better understanding of host preferences, 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 have begun.

Human malaria, both P. falciparum and P. vivax have been successfully transmitted to gibbons both by whole blood inoculation and by the inoculation of sporozoites from infected mosquitoes. Preliminary treatment studies indicate that the gibbon will be a useful experimental animal for this purpose also. Unfortunately, except from the gibbon's viewpoint, there is no clinical disease accompanying the infection in gibbons.

Further immunologic studies including fractionation of antibodies are being done on monkey malaria.

## MELIOIDOSIS

Melioidosis is a disease of man and animals caused by a bacterium called Pseudomonas pseudomallei. The disease is polymorphic; almost any symptoms may be presented, from mild abscesses to a rapidly fatal septicemia, from diarrhea to fairly chronic lung disease and it is thus impossible to diagnose on clinical grounds alone. The distribution of the disease is virtually restricted to Southeast Asia. It is a relatively rare disease which the textbooks consider to be highly fatal. Some evidence that subclinical infection with the causative agent may be more common was suggested by a small serological survey in Thailand. In neighboring Malaysia and Vietnam, Pseudomonas pseudomallei has been found to be widely distributed in soil and water. At the time this SEATO study was initiated there was essentially no information about the presence of the organism in Thailand or its importance as a disease agent in man and animals although a few human cases had been reported in Thai medical literature. 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 organism has been isolated have antibody against the organism whereas in those areas from which the organism could not be isolated the people do not have antibody. Thus, it appears that Pseudomonas pseudomallei is a more benign organism than was formerly thought and might be regarded primarily as a saprophytic opportunist. We have yet to find an active case of disease although the widespread presence of the organism makes it necessary to consider melioidosis in the differential diagnosis of infectious disease in Thailand. Prompt bacteriological diagnosis may be life-saving in the rare cases which may arise.

## MOSQUITOES

SEATO Medical Research 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 a 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, Aedes aegypti, 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 repellants 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 in malaria and dengue control programs. Cooperative studies with the Royal Thai Army and the United States Department of Agriculture are being 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.

## NEUROLOGY

The primary area of interest is the involvement of the central nervous system by infectious diseases, not just those which are usually thought of as neurologic diseases, but other systemic illnesses such as malaria. This includes not only the acute involvement but the long term sequelae as well.

Most of the work so far has been devoted to cerebral malaria. (This is discussed under the heading of Malaria). Studies will include all the techniques available; clinical, chemical and electrical measurements. These studies will later be extended to include other tropical infectious diseases.

Secondary emphasis is placed on the general neurologic problems to be found in Thailand and to assist local physicians in defining the magnitude of the problem.

## NEUROPSYCHIATRY

The neuropsychiatric studies which were recently initiated have the goal of defining how 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 select communities concerning the effect of the introduction of modern medical practice is underway or will soon be initiated. These studies are being carried out by a staff of two psychiatrists and one social anthropologist assigned to SMRL and by two social anthropologists associated with the laboratory through Army R&D contract.

The studies of transcultural communication, and advisor-counterpart relationships is being designed and carried out as a social psychiatric study of the factors influencing information exchange and performance in a situation where representatives of different cultures are required to collaborate in the accomplishment of tasks. Factors such as differences in value commitments personal psychology, language skills, and interpretation of task definition will be studied in JUSMAG Army Sections. A similar study proposes to focus on problems in transcultural communication and changes in medical student behavior in Chiangmai where U.S. medical educators are cooperating with the Thai faculty in the introduction of new teaching techniques.

Another study will investigate the adaptational problems presented by American families with the hypothesis that adaptational patterns predicated upon the existence of certain cultural forms may be ineffective when applied under different environmental conditions.

In addition to the social psychiatric studies, the three anthropologist are carrying out studies of problems associated with the expansion of rural health services in Thailand. They are working in a central Thai village (Lao Khwan), a North Thai community near Chiangmai and in a Karen-Meo area in Amphur Samerung where they are studying practices related to health and disease with the context of the total culture. It is anticipated that these investigator will collaborate with a psychiatrist in carrying out an epidemiologic survey of health problems. One purpose of this survey will be to establish the form and frequency of complaint patterns and to investigate how the group under study attaches practical social significance to a given complaint pattern. It is the goal of these studies to establish the factors which influence the definition of health and disease within the context of the total culture.

## NUTRITION AND METABOLISM

Nutrition is one of the major problems in Thailand, especially in children. The ICNND\* survey in 1960 revealed that considerable thiamine deficits (dietary survey and biochemical study) were found among the civilians, but clinical beri-beri was not observed. The ICNND survey had no adequate information regarding thiamine nutrition in infants, pregnant and lactating women. How long a person is stress, both physical such as a fighting soldier and physiological such as during pregnancy and lactation, can tolerate marginal thiamine nutrition is unknown. The role which thiamine deficiency plays in the high mortality among infants and small children is also unknown.

Thiamine nutrition in pregnant, lactating women and their infants was evaluated by physical examination and biochemical determination, including erythrocyte transketolase activity, thiamine content of urine and milk. Attempts have been made to correlate the clinical status and biochemical findings as well as to find the best biochemical test to detect sub-clinical thiamine deficiency. Studies were carried out in Chiangmai (North), Ubol (Northeast), Songkhla (South), and Bangkok (Central). Data indicate that lower serum protein, hemoglobin and hematocrit are observed in Ubol and Chiangmai as compared to Songkhla and Bangkok. Erythrocyte transketolase and urinary thiamine level are low or deficient in about 30% of studied subjects in Chiangmai and Ubol, and about 10% in Songkhla and Bangkok. Thiamine content of human milk from Songkhla is significantly higher than the other 3 areas ( $p < 0.01$ ). Study of a better economic group of subjects living in Bangkok is in progress. A possible role of thiaminase in the etiology of beri-beri in Thailand is currently being investigated.

Riboflavin deficiency also exists in Thailand. A rapid, reliable diagnostic test for riboflavin deficiency is being investigated. Thus far, methods for the quantitative extraction and microbiological determination of tissue flavin have been developed.

Arcus Senilis is commonly found in Thais, even though the average cholesterol from many areas around Thailand was only 132 mg% (ICNND survey in 1960). In the U.S., the presence of arcus senilis is frequently accompanied by an elevated serum cholesterol. It will be important to discover if a similar association exists here. Study is in progress and no conclusion can be drawn at present time.

Vitamin A intake is low and serum vitamin A level correspondingly so. The relationship between vitamin A serum level and vision as tested by an Electroretinogram has been evaluated in the Ubol Province. No conclusion can be drawn at present time.

\*ICNND - Interdepartmental Committee on Nutrition for National Defense.

## RABIES

Rabies is a disease of major importance in Thailand. In 1963 for example, fifty human cases of rabies were reported in the city of Bangkok. Estimates for the provinces range up to 4 times this figure. The Thai Government has proposed a canine immunization program for Bangkok, however this program has not yet been instituted. In other provinces no such program has been proposed. There is a program to pick up and destroy stray animals in Bangkok but this is very difficult to accomplish. No information is available on the wildlife reservoir of rabies in Thailand or on the spread from village to village. Bat rabies had not been previously reported in Thailand. Current methods of diagnosis of this disease are mouse inoculation and Negri body stains. In addition the fluorescent antibody rabies test is used in this laboratory. Efforts will be made to detail the prevalence and distribution of domestic rabies throughout Thailand. The prevalence of sylvatic and bat rabies will be investigated.

Rabies has been isolated in dogs from all provinces where specimens have been obtained including provinces where previously rabies was not known to exist. In a few provinces where specimens have not been obtained, the local veterinarian has reported clinical diagnosis of rabies. Rabies virus has been isolated from dogs, cats, cows, gibbons and insect eating bats. In a study at Udorn, 3 of 44 dogs picked up by Local Public Health authorities from the morning market area were positive for rabies. Future studies will be directed towards better delineation of non-domestic reservoirs of rabies.

## RENAL STUDIES

Renal studies have thus far been aimed at identifying normal physiologic processes in Thai subjects. Detailed renal function studies have been performed on 51 adult patients and 16 children. These studies include measurement of diurnal variations of electrolytes, pH, and creatinine; concentrating ability; phosphate clearance; PSP excretion; and clearances of inulin, PAH and creatinine. When these baseline studies are completed, studies of a variety of disease processes are planned. They include at the present time Thai hemorrhagic fever, malaria and nephrosis. Indeed a study of this latter condition is already underway. Fourteen cases proven by biopsy have undergone renal function studies thus far.

## RESPIRATORY VIRUS

Influenza in epidemic form was seen in Northeast and North Thailand in September and October 1965. An A-2 (Asian) strain was isolated from several cases and is presently being studied for its antigenic relationship to other A-2 strains. Preliminary studies indicate a close relationship to recent A-2 strains from the U.S.

An outbreak of Herpangina in Bangkok was proven to be due to a Coxsackie A virus and clinical and virologic studies of cases seen at Childrens Hospital are being done.

Adenoviruses of at least three different types have been isolated from febrile respiratory disease cases in children in Bangkok. Diagnostic studies of febrile URI's in children and US troops are continuing to determine the types of adenoviruses common in Thailand .

## ZOONOSES

Zoonoses are of great economic and public health importance to the Thai people. Diseases such as anthrax produce deaths in both the human and domestic animal population in Thailand. Anthrax in humans is of the gastrointestinal type and occurs in village epidemics due to eating infected buffalo meat. Trichinosis has been reported as the cause of human deaths in the Central Plains area of Thailand. Much information is also obtained by study of tissue pathology associated with disease in domestic animals from various areas of Thailand.