

Research into Disease - II

**THE SEARCH
FOR HEALTH**

**SEATO Medical Projects
in Thailand**

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**SEATO Medical Projects
in Thailand**

Text by **Barbara Kris**

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H.M. the King of Thailand lays the foundation stone of the SEATO Clinical Research Centre's new building on SEATO's tenth anniversary, September 8, 1964.

The Purpose of Research

Men, women, and children are the critical resource of any nation; in a developing nation such as Thailand, human resources are the mainspring of social improvement, economic progress, and political survival. It is the initiative and know-how of the people that changes a low-income country into a modern nation; but, education and opportunity are needlessly wasted if disease saps people of the ability and the desire to strive – both for the nation and themselves. A man with malaria may find that only a few hours of fishing or cultivating each day are possible. A child with chronic dysentery is a listless student.

The South-East Asia Treaty Organization, as a group of eight nations pledged to promote progress and well-being, sponsors three medical research projects: the SEATO Medical Research Laboratory, the SEATO Clinical Research Centre – both in Bangkok, Thailand; and the Pakistan-SEATO Cholera Research Laboratory in Dacca, East Pakistan. These projects have several purposes: medical research, health education, improvement of methods of medical care, and training of clinical and research personnel – four ways to help Pakistan, Thailand, and nations around the world husband their human resources.

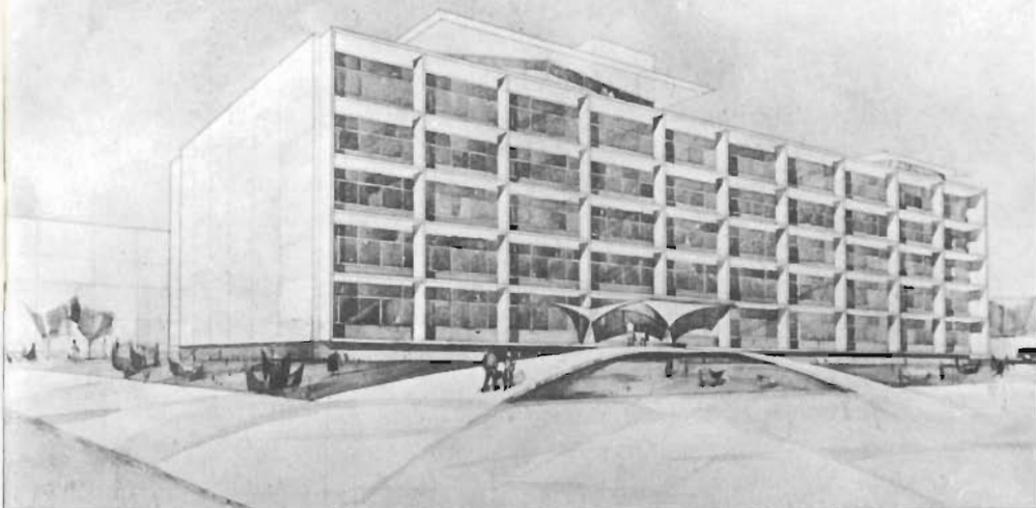
This publication describes the Organization's program in Thailand – the SEATO Medical Research Laboratory and the SEATO Clinical Research Centre. A companion booklet tells of the Pakistan-SEATO Cholera Research Laboratory.

History of the Projects

In 1958 and 1959, Thailand was struck twice by severe cholera epidemics. The nation's need for assistance was apparent when the SEATO Council of Ministers met in April, 1959, at Wellington, New Zealand. It was agreed that SEATO would sponsor a cholera research project in Bangkok. By December 1959, a laboratory had been established under the joint guidance of the Royal Thai Government and the National Institutes of Health in Washington, D.C. The laboratory was staffed by medical personnel from the Thai and United States armed forces.

By April 1960, happily, Thailand no longer needed an emergency cholera research program, although the need for long-term cholera research remained. At the SEATO Council meeting at Washington in that month, it was decided to move the cholera research project to Dacca, East Pakistan, and in its place establish a medical research laboratory in Bangkok to deal with other diseases — both numerous and serious — that undercut efforts toward social and economic advance in Thailand. An exchange of diplomatic notes between the Governments of Thailand and the United States put the Council's decision into effect on December 23, 1960. The new laboratory was staffed by a Thai Component from the Ministry of Defence and a U.S. Component which is a Special Activity of Walter Reed Army Institute of Research in Washington, D.C.

The Laboratory quickly outgrew its quarters on one floor of the Royal Thai Army Institute of Pathology building. A new four-storey building was completed in 1962, a large animal house was added, and sizeable portions of the School of Tropical Medicine and the School of Public Health buildings were given over to the Laboratory's activities. Studies in veterinary medicine were established with the Department of Livestock Development of the Ministry of Agriculture. Yet none of these developments completely satisfied a growing need which follows naturally from laboratory medical re-



CLINICAL RESEARCH CENTER : SEATO MEDICAL RESEARCH LABORATORY : BANGKOK

*Architect's impression of the SEATO
Clinical Research Centre building.*

search; the need for clinical research facilities. As a stop-gap, the Royal Thai Army Hospital and the Children's Hospital provided these facilities, but the need for space to develop clinical research remained.

In April 1963, a second exchange of diplomatic notes between the Governments of Thailand and the United States established the SEATO Clinical Research Centre. Its establishment, again, began in the SEATO Council. Thailand and the United States agreed to provide financial support. Matters of program and personnel are determined by the University of Medical Sciences in Bangkok and the Walter Reed Army Institute of Research, Washington, D.C. There is an organizational and functional relationship between the Centre and the Laboratory. The Centre provides clinical facilities for research concerning diseases under study by both the Centre and the Laboratory. It has special facilities for the study of heart disease, metabolism studies, and investigation of nutritional diseases of Thailand.

Organization

Both the SEATO Medical Research Laboratory and the SEATO Clinical Research Centre are parts of the medical research program of the South-East Asia Treaty Organization, which in council takes major policy steps, such as the decisions to institute, first, the cholera project, then the Laboratory and the Centre. The work of making the Council's decisions viable falls to representatives of the SEATO Secretary-General, the Directors-General of the Laboratory and

Pressing a button to unveil the name plaque, the Prime Minister of Thailand, Field Marshal Thanom Kittikachorn, dedicates the SEATO Medical Research Laboratory's new building in Bangkok. Others in photo, from left to right, are: Mr. Konthi Suphamongkhon, Secretary-General of SEATO, 1964-65, Mr. Pote Sarasin, Minister of National Development and formerly Secretary-General of SEATO, Air Chief Marshal Dawee Chullasapya, SEATO Military Adviser for Thailand, Major-General Pung Pintuyothin, Director-General of the Laboratory, Colonel James L. Hansen, Director of the Laboratory's U.S. Component, and Captain Samrit Jatinandana, Deputy Director of the Laboratory's Thai Component.





The SEATO Medical Research Laboratory.

Centre (representing the Thai Government), and the U.S. Army Medical Service. Executive functions within the Laboratory and Centre are shared by the directors of the various components.

The Laboratory has two divisions. The first, the Division of Medical Research Laboratories, has departments of Bacteriology and Immunology, Geographic Pathology, Medical Zoology, Medical Entomology, Virology, and Veterinary Medicine. The second is the Division of Special Projects, with sub-divisions based on diseases or subjects being studied: malaria, rickettsial diseases, amoebiasis studies, MAPS (Migratory Animal Pathology Survey) project, and social anthropology.

The Clinical Research Centre has executive and scientific operational staffs, and areas of investigation are: nutritional studies - initially thiamine deficiency and metabolism; anaemias - studies of haemoglobin types and enzyme-deficiency; heart disease; malaria; and bladder stone research. These projects create the framework for the research now being done, but this will probably be modified in form and function with project changes to include many diverse clinical research problems in South-East Asia.

Staff and Facilities

The professional staffs of the Laboratory and Centre are composed of Thai and U.S. military and civilian personnel. Technicians and research fellows are from Thailand and the United States, and in a few cases candidates for advanced degrees at universities in Thailand conduct research for their theses, which is correlated with the Laboratory's and Centre's current research program. It is hoped that students and technicians from other member nations of SEATO - and non-member nations - will come to the Laboratory and Centre to help in its work and to receive training in research and laboratory techniques.

In 1964 the new four-storey building located beside the Royal Thai Army Hospital was completed and equipped, giving sorely-needed laboratory and office space for the rapidly-developing research work.

The Laboratory's work is also carried on beyond the Bangkok-Dhonburi metropolitan area. Temporary field stations are set up when required by research projects. Collection of animals may require this, or it may be the outbreak of a particular disease, as in the case of the occurrence of anthrax in Cholburi.

The decision by the Thai and U.S. Governments to construct and equip a new building for the Clinical Research Centre brings together work that has been carried on in buildings spread across Bangkok. Until 1965, the large biochemistry and nutrition laboratory had been at the outskirts of the city, a second biochemistry laboratory in the Medical Research Laboratory, yet another laboratory in the Royal Thai Institute of Pathology building, and the Cardiac Catheterization Clinic and the Thai Haemorrhagic Fever Ward in the Phra Mongkut Klao Hospital. Facilities have been scant and scattered for the Centre's current projects; the need to expand the research program is pressing.

The SEATO Clinical Research Centre, completed structurally in 1965, is an excellently-equipped five-storey building. The wards accommodate forty patients, chosen from other hospitals in Bangkok and outlying areas. The biochemistry laboratories form the core of the Centre's work, and there are also diagnostic procedural facilities, operating rooms, X-ray equipment, and a radioisotope section. The Cardiac Catheterization Clinic is in the Centre's new building. The Centre's equipment affords facilities for testing and medical research that, in many instances, cannot be found elsewhere in South-East Asia.

Research in Progress

Research at the SEATO Medical Research Laboratory and the SEATO Clinical Research Centre will be categorized in this booklet by disease rather than by division or department, because research concerning a single disease is infrequently the domain of a single department. For example, the group studying malaria within the Division of Special Projects is assisted in its work by the departments of Medical Entomology, Geographic Pathology, and the Clinical Research Centre. Not only is the work done within the Laboratory a co-operative effort among departments, but, also, the Laboratory's and Centre's work interlocks. Projects often require the professional attention and equipment of several divisions.

SFC John Tabalevsky takes blood smears from children in a village of Satul Province, southern Thailand, for the study of malaria.

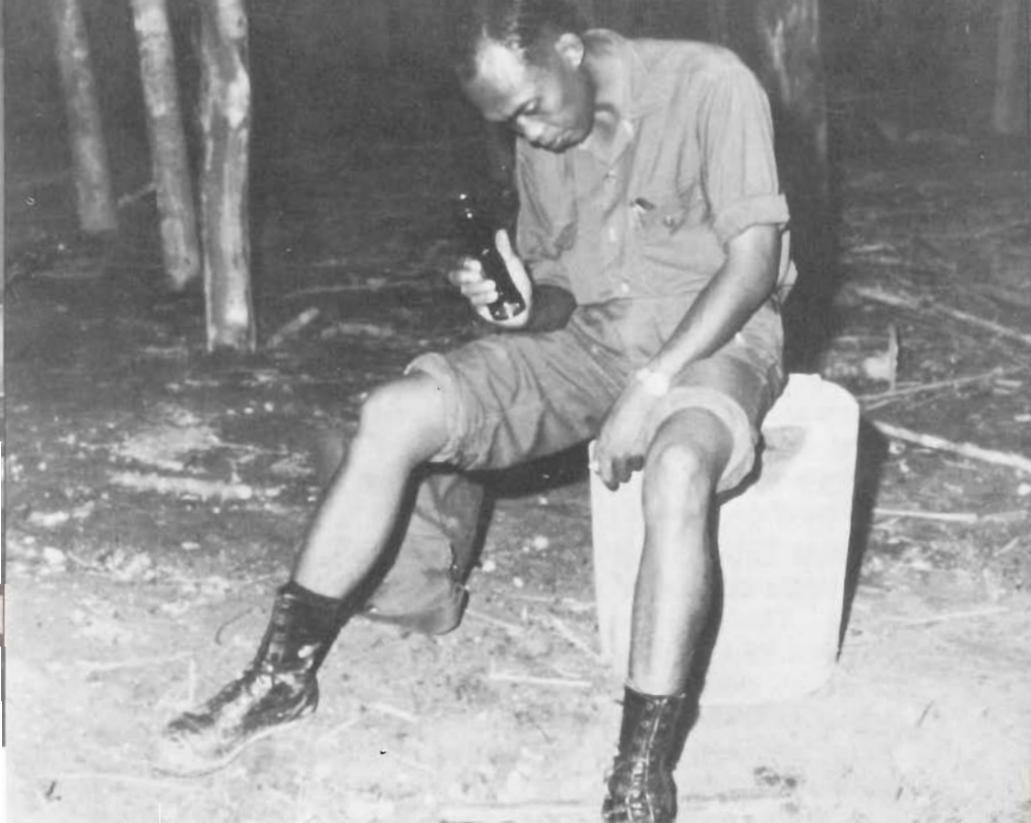


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"Catch it before it bites!" Members of the Department of Entomology's teams, like Mr. Sahem Esay (show here) have become expert in using themselves as "live bait" for mosquitoes which are collected in bottles and sent to the laboratory. The object is to catch anopheline mosquitoes, which transmit malaria, for research purposes.

Malaria

Judging by the number of cases and their severity, malaria is one of the most serious diseases in Thailand. Dense rain forest, permanently swampy areas, standing water in southern Thailand and uncleared forest and scrub in the north and east stubbornly resist the control of malaria and other arthropod-borne diseases.

The Laboratory's Division of Special Projects is studying drug-resistant strains of malaria and their geographic distribution. The Department of Medical Entomology cooperates in

the study of the malarial mosquitoes' behaviour and of the effect of DDT on these carriers.

A variety of drug-resistant types of malaria are found in Thailand, the rest of South-East Asia, and parts of South America. In Thailand there are malaria parasites resistant to chloroquine, the most common drug currently used in the treatment of the disease, but quinine can be used successfully. However, drug-resistant types appear to be increasing, and, in Viet-Nam, there is a type of malaria which will not respond to treatment either with chloroquine or quinine. Although other drugs can be used in the treatment of malaria, there is no certainty that they will be effective with all strains of drug-resistant malaria.

The Laboratory is working to discover how the strains of malaria existing in Thailand will respond to the available drugs. This study also includes identification of the vectors, the geographic distribution of malarial strains, and the response of mosquitoes to sprays. Identification of resistant strains involves testing blood samples from patients to determine whether these are truly cases of drug-resistance or if the drugs are ineffective because of metabolic peculiarities of the patient.

The Laboratory's work toward cure and control of malaria will have social and economic consequences. Life expectancy will rise following a decrease in deaths from malaria itself and in deaths from other diseases which become fatal in a patient weakened by successive attacks of malaria. In the economic sector, the end of malaria in Thailand will probably be marked by a rise in per capita agricultural production. Malaria is more common among rural than urban workers, and in the past, agricultural production increases have been noted in countries successful in controlling malaria.

Studies which may assist in eradicating the ever-present pest mosquitoes are linked with the study of malaria vectors.

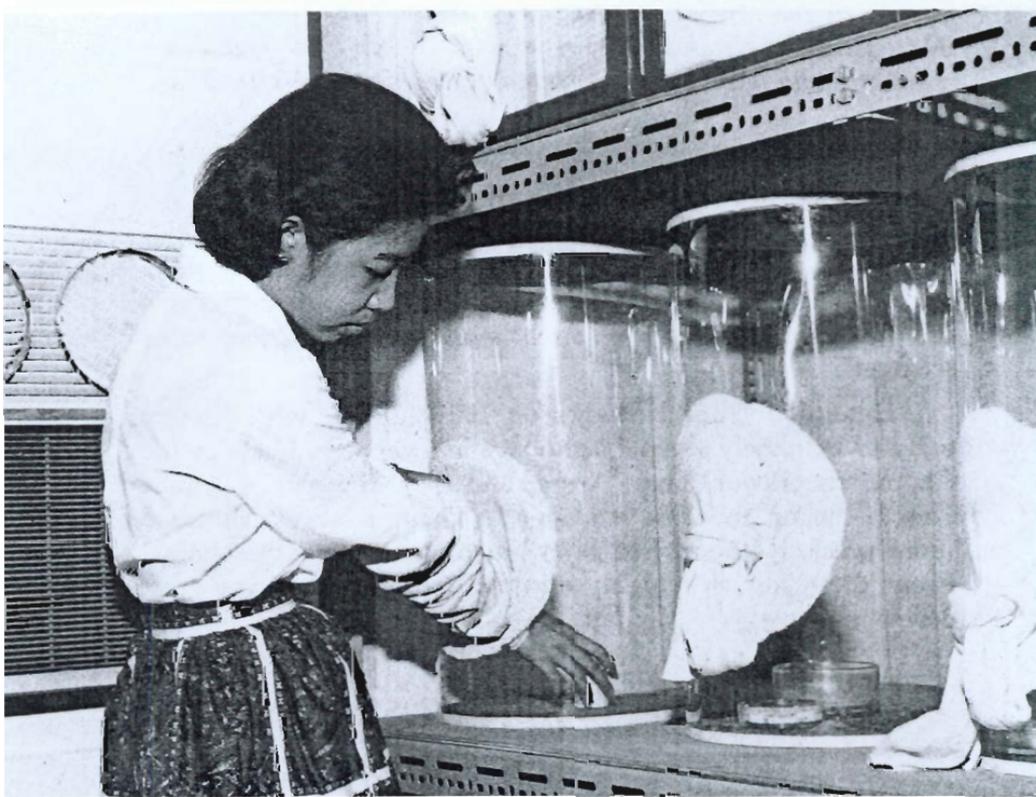
Thai haemorrhagic fever

A second mosquito-borne disease of importance in Thailand is Thai haemorrhagic fever. This disease only attacks children and is fatal in about ten per cent of the cases. A

moderate fever of 101° – 103°F lasts five to fifteen days, and other early symptoms include hypotension, weak pulse, clammy skin, cough, abdominal pain or tenderness, vomiting, restlessness, and apprehension. In the advanced stage there is escape of fluid through the weakened walls of the circulatory system and, finally, complete collapse of the cardiovascular system. There is no known prophylaxis other than using repellents to avoid mosquito bites.

The Laboratory's research has resulted in identification of the virus and of the vector, the mosquito *Aedes aegypti*. It has also been shown that, oddly enough, the disease attacks only Oriental children. Caucasian children living in Thailand have never contracted the disease, although the same virus that causes haemorrhagic fever among Thai children has been shown to cause dengue fever among Caucasians, a disease much like the old-fashioned grippe and which is not fatal. As yet, it has not been determined whether susceptibility has an environmental or hereditary cause. The Laboratory's and Centre's investigations have indicated that diet and living condi-

Miss Supanee Sandhinand working with a laboratory colony of anopheline mosquitoes.





Major Scott B. Halstead, whose contributions to knowledge of haemorrhagic fever have aroused wide medical interest, shown in the virology department of the Laboratory with Dr. Ananda Nisalak, one of a number of Thai research workers who have been associated with him in his studies.

tions are not directly related to the incidence of cases of the disease. Children from both high and low-income families contract haemorrhagic fever. This question of whether there is an environmental or a hereditary cause is of continuing interest to the medical research worker, and to the social scientist.

Extensive clinical studies on 160 children with moderately to extremely severe haemorrhagic fever were made by the Centre, the Royal Thai Army, and the Ministry of Public Health during the 1964 epidemic. These studies delineated more precisely the altered body functions leading to collapse. From these results a highly effective treatment regimen was developed.

Viral hepatitis

Viral hepatitis is an acute, infectious disease causing inflammation of the liver. This is accompanied by headache, loss of energy, the feeling of being "washed out", and jaundice. The only prophylaxis available is human gamma globulin, which is limited in quantity. Bed-rest and a low-fat diet are the present treatment, with convalescence usually stretching over many months. The sole method of prevention is a high level of personal and public hygiene and sanitation.

The Department of Pathology is studying viral hepatitis in conjunction with their study of other liver ailments in Thailand. Through their research they hope to discover if viral hepatitis in Thailand differs from the disease elsewhere in the world.

Poliomyelitis

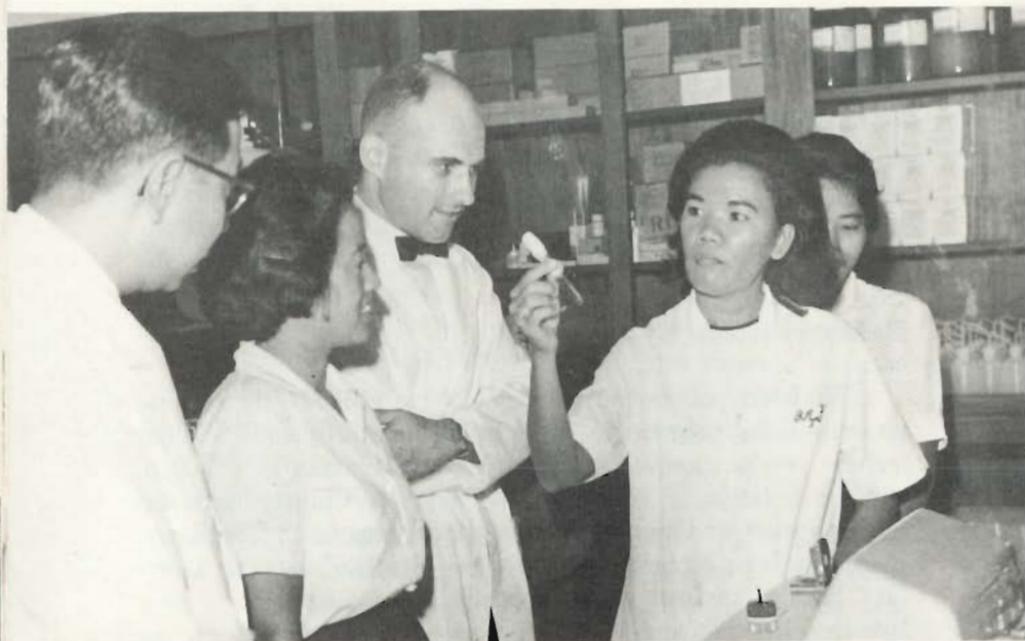
Work on poliomyelitis and associated viruses – the enteroviruses – is in progress in the Virology Department. Studies include yearly surveys of poliomyelitis antibodies in children and the isolation of viruses from Thai and Chinese children with a variety of illnesses. An outbreak of polio in Vientiane, Laos, has been studied and the virus identified as type 1 polio. Similar studies are being conducted on Americans who live in Thailand and have diseases which are difficult to diagnose.

Venereal disease

The Department of Bacteriology has begun investigations of venereal disease in Thailand. At present, research is concerned almost wholly with gonorrhoea, the most prevalent of venereal diseases in South-East Asia.

Since 1955, gonorrhoea has shown increasing resistance to treatment with penicillin, and dosage has had to be increased. These more stubborn gonorrhoea bacteria, although found all over the world, can be traced to Asia.

Resistance to treatment may arise from any of three conditions. The first is the use of a type of penicillin with which an adequate level in the blood cannot be achieved or maintained long enough. The second is re-infection. The third is, as yet, conjectural; some organisms, such as staphylococci, form an enzyme called penicillinase. This enzyme counteracts penicillin, making it ineffective. The Department suspects that



gonorrhoeal bacteria can help form this enzyme, and there are plans to investigate this possibility.

The Department is testing a number of possible drug regimens for the treatment of gonorrhoea – combinations of penicillin, tetracycline, and other drugs. This is done by isolating organisms and testing their drug sensitivity in the laboratory and by using the several drug regimens in treatment of patients. In the future they hope to discover the minimum dosage and the least expensive drug regimen that provides a certain cure.

Japanese encephalitis

Japanese encephalitis is another viral disease transmitted by mosquitoes. It is often confused with African sleeping sickness, as the two diseases have similar symptoms. The disease occurs throughout the area stretching from Japan to India, but it is called "Japanese" encephalitis because the virus was first identified in Japan. There is neither preventative nor curative medication, and the disease is often fatal; surviving victims suffer debilitating brain damage. The Departments of Virology and Medical Entomology have been trying to isolate Japanese encephalitis from mosquitoes in two regions of Thailand: Bang Phra in Choburi province and

Medical staff associated with the haemorrhagic fever study centre at Phra Mongkut Klao Hospital, Bangkok, inspect new equipment. The ward, opened in 1964 by the Ministry of Public Health, draws its support from the Department of Health and Medical Services of the Ministry, the Royal Thai Army Medical Service, the medical universities, and the SEATO Medical Research Laboratory and Clinical Research Centre. Left to right: Dr. Aree Valyasevi, Chief of the Thai Component, SEATO Clinical Research Centre, Dr. Pornrat Indrakoses, Pitsanuloke Hospital, Captain Sanford Cohen, Coordinator for the U.S. Component, SEATO Clinical Research Centre, Lt. Col. Majuri Balankura, head of the study centre, and Dr. Mallika Tumrakdee, of Rajburi Hospital.

Pak Kret in Nondhaburi province. It has been determined that in Bang Phra the mosquitoes *Culex gelides* and *C. tritaeniorhynchus* are important carriers. Also it has been noted that Japanese encephalitis is present in those areas during October and November, the months in which the populations of the two carriers are at their peaks.

In addition, the roles of birds and animals as virus reservoirs are being studied, and bird and animal collections have been made in most parts of Thailand.

In 1964, an outbreak of Japanese encephalitis was recognized in Thailand for the first time. One hundred cases admitted to Pitsanuloke Hospital have been confirmed by laboratory tests, and it is likely that many more cases have occurred.



A swallow trapped in Yaowarad Road, Bangkok, is gently taken from the net by Dr. Joe Marshall, leader of a team from the Laboratory which is making a survey of the birds of Thailand. Over 20,000 swallows were banded and released in Bangkok as part of a project to establish whether or not birds have any significant place in the spread of disease.

Liver fluke

The Department of Medical Zoology, at the field station at Udorn in north-east Thailand and with field teams sent throughout the country, is studying human infestation by the liver fluke *Opisthorchis viverrini* and this fluke's life cycle. Fifteen per cent of the Thai population is infected by the parasite, and 3.5 million of the victims live in north-east Thailand – 90% of the population there. This concentration of the infected in one region has a cultural cause; raw fish is a favourite complement to the diet of rice and vegetables, and the Department has proven that the eating of raw fish is the way in which humans become infected with the fluke.

It has been found that the fluke eggs reach ponds and streams via human faeces. There, certain species of snails eat

the eggs and, after a period of development, free-swimming larvae leave the snails and penetrate fish. When these fish are eaten raw or improperly cooked, the larvae become adult worms in the human liver.

The obvious answer is: Don't eat raw fish. Unfortunately, the problem cannot be solved so easily. Although the Department spends endless time and patience in trying to convince people that their fish should be cooked, their efforts have gained only partial success. The people cannot yet fully understand why they should not eat raw fish. The reason is a human one. They are very fond of raw fish, and it will take more than the word of a stranger to convince them of its danger.

This resistance necessitates the Laboratory's trying to eradicate liver fluke in the waterways. They are hoping to break the life cycle at some point, and the attempt to identify the snail carriers is directed toward this end. Each month about 150,000 snails are collected and sent to the Laboratory in Bangkok for examination. Indigenous wild animals are also trapped and sent in to determine if they are significant in the fluke's life cycle.

Laboratory workers search for water snails – carriers of liver fluke – in a muddy pool in North-East Thailand.



The Department of Pathology is studying clinical and biochemical changes in the liver and the bile system which result from fluke infestation, and 1,100 people in Udorn have been examined by the Department of Medical Zoology. Assessing the effects of the fluke is complicated by the fact that many victims are also suffering from other liver ailments, such as cirrhosis, cancer, and viral hepatitis. The Laboratory is also studying whether the presence of fluke may have a causal relationship with these other diseases and with malnutrition, common in Thailand because of improper diet.

The Laboratory is not only trying to discover preventative measures, but curative ones as well. Drugs are being tried on animals and human volunteers, but it appears that more drugs must be tested before one is found that will kill the worms in the bile ducts without producing harmful reactions.

Lung fluke

The fluke *Paragonimus westermani* can infect the lungs of man and certain animals. It is known that this fluke is ingested by eating raw or improperly cooked crab meat. The extent of infection in Thailand is still uncertain, although the presence of the fluke has been proven in both human and animal populations. The Department of Medical Zoology has determined that 15% of the domestic cats in north-east Thailand have another species of lung fluke, as do tigers captured in southern Thailand. Humans have been given skin tests, and those having positive reactions have been tested further. In central Thailand, about 50 human cases of lung fluke infestation have been found by other investigators.

Snails and crabs are the known hosts, but the species responsible in Thailand are still undiscovered. The Department has examined many thousands of crabs and snails in an effort to find the vector. Several larval forms of flukes have been found in crabs and have been fed to experimental animals. This work is still in progress.

The Laboratory's lung fluke research is continuing. A species found in animals in the north-east was not previously known, and it is now being fully described.



Tasty - but dangerous. Major Dale E. Wykoff points out the risk of liver fluke infestation to a Thai girl preparing a meal of raw fish in a North-East village.

Blood flukes

An unusual form of human blood fluke was found in the far south of Thailand. Since then, the Department of Medical Zoology has found one case in the north central area and another in the north-east. The snail intermediate host has not yet been found, and it must be determined if this parasite is *S. japonicum* or if it is another type. Adult blood flukes have, for the first time, been obtained from rats in the north and north-east.

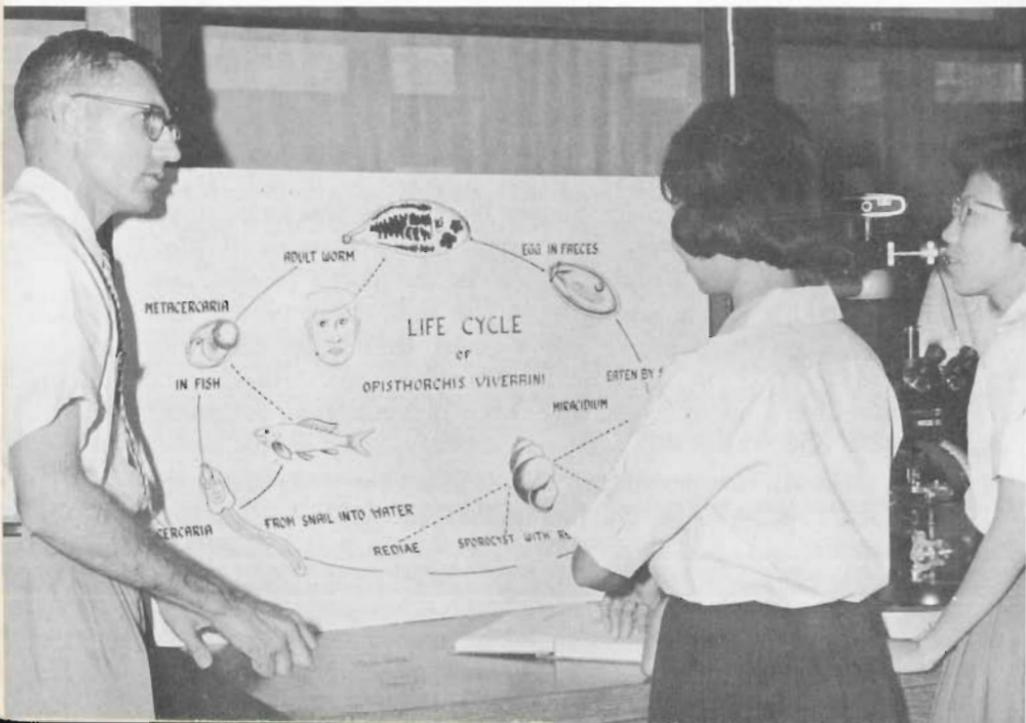
Blood fluke research in Thailand is at an early stage, and much remains to be done now that the problem has been presented.

Rickettsial diseases .

Research projects at the Laboratory are collaborative ventures in which Thai and other SEATO investigators join forces. The rickettsial section within the Division of Special Projects is staffed and directed largely by Thais. This group is studying the distribution and density of scrub typhus. The disease is characterized by fever and skin rash and is transmitted to man by chiggers (red-bugs or harvest mites). Although there is a cure for it, in rural areas the disease often goes undiagnosed and untreated because of inadequate medical facilities and a shortage of medical personnel. The Department of Medical Entomology helps in the study of rickettsial disease by examining ectoparasites found on wild mammals of Thailand.

There is no vaccine for this disease, but, hopefully, research will produce one. Although effective insect repellents exist, they are bothersome to use, requiring rather tedious and

A chart showing the life cycle of the liver fluke is shown by Major Dale E. Wykoff to two of the Laboratory's technicians. Major Wykoff was in charge of this aspect of the Laboratory's research work.



No harmful effect usually follows infection by five kinds of amoebae which live in man's intestine. A sixth amoeba, *Entamoeba histolytica*, causes mild amoebic diarrhoea, the dangerous amoebic dysentery, and amoebic liver abscess, the latter two of which can be fatal. The amoebiasis section of the Division of Special Projects and Thai investigators in other

Amoebic dysentery and amoebic liver abscess

Future research in rickettsial diseases will include determination of the species of ectoparasites which serve as carriers and of the mammals which may serve as reservoirs for rickettsiae or as alternate hosts for the ectoparasites. Efforts are also being made to improve methods of diagnosis and control.

Prevention of scrub typhus. In effect, there is still no practical answer to the mass time-consuming application every four hours. Few people would be willing or able to use these repellents faithfully around the

In classifying potential disease carriers, the Laboratory has undertaken extensive animal trapping operations in various parts of Thailand. Here, laboratory workers look for suitable places to set their traps.



laboratories believe that in addition to the active cases of diarrhea, dysentery, or liver abscess, a great number of the local population carry this amoeba without ill effect. It is this relatively large number of healthy carriers that form the reservoir for spread of *E. histolytica* which in a new human host may cause disease. This microorganism is relatively rugged and can survive ordinary water chlorination. Also, infection can follow eating of uncooked food or food contaminated by a person carrying the microorganism. Amoebic infection occurs throughout the world and may be particularly prevalent and dangerous in tropical areas.

The infection can spread from the intestine. Occasionally the brain is invaded, and the disease is then fatal. Spread to the liver is much more frequent and results in liver abscess; recovery is usual if diagnosis is made and energetic treatment begun.

One approach in the Laboratory's research is the attempt to cause the disease artificially. The amoebae are isolated and grown in colonies for intensive study. Scientists at the Laboratory are testing the hypothesis that *Entamoeba histolytica* requires an assistant—perhaps another organism, a chemical, or a condition—before disease is produced. This, of course,

The counting of colonies of bacteria from a patient with acute diarrhea being carried out by Miss Chantana Bhadhana-band in the Department of Bacteriology and Immunology.





Cholera, the original subject of research in Bangkok, is still under investigation. Dr. Richard Finkelstein, whose work is mainly concerned with the part played by cholera toxin in the onset of cholera, with his co-worker, Dr. Pongsom Atthasampunna.

would account for apparently healthy carriers. A wide range of experiments are being conducted to simulate disease-causing conditions. When these answers are found, perhaps there can be found also a method of combatting this disease in Thailand and the rest of the world.

Bacterial diarrheas

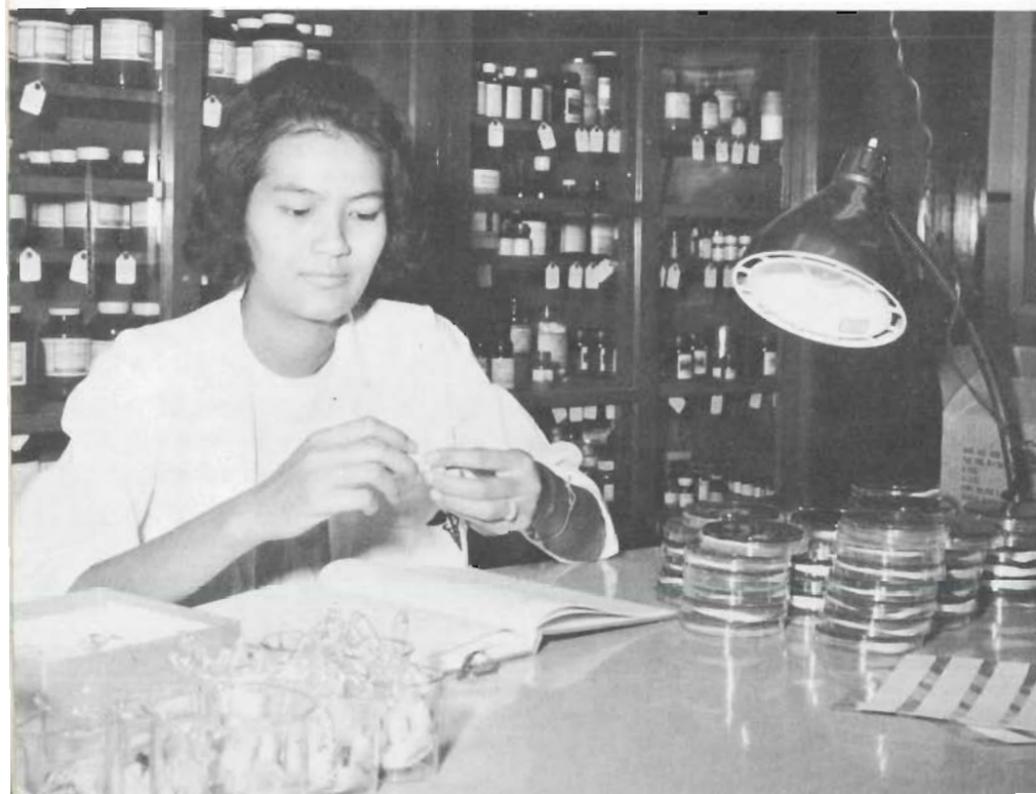
Bacterial diarrheas are under study in the Department of Bacteriology and Immunology. Many bacteria live in man's intestines and are benign or beneficial. Others cause diarrheal diseases with symptoms ranging from mild and shortlived diarrhea to repetitive and severe diarrhea, acute abdominal pain, the passing of blood, dehydration, and death.

Basic studies in such diseases include isolation and enumeration of intestinal flora and investigation of the mechanisms

of diarrheal toxins. This basic work will help explain the complex causes of diarrheas and will contribute to the development of vaccines and therapy for the correction of intestinal flora imbalance.

Other investigations cover the identification and characterization of diarrheal bacteria – varieties being much more numerous in Thailand than in Western countries – detection of the source, and interruption of the often indirect path by which the disease bacteria get from the intestines of one individual to the intestines of another. The Department's work in identification is particularly important during epidemics of diarrheal diseases, such as cholera. Bacteria-bearing samples are sent to the Laboratory for identification, an essential step in the treatment of the disease. The Laboratory's introduction of fluorescent microscopy cuts the time required for identification from two or three days to less than one.

Dr. Chiraphun Duangmani, of the Laboratory's Department of Bacteriology and Immunology examines a vial of dried cholera organisms. The Laboratory maintains a collection of bacteriologic cultures indigenous to South-East Asia.





Dr. Howard E. Noyes, Chief of the Department of Bacteriology and Immunology and his assistant chief, Dr. Richard H. Finkelstein, examine cultures of bacteria with a stereoscopic microscope.

For use during epidemics and for the Laboratory's regular research work, the Department has developed a transport medium for the conveyance of bacteria samples. This jelly-like substance stays fresh for months and enables perishable bacteria samples to survive for a number of days in transit.

The Department has also found that control of diarrheal disease is complicated by the human carriers who remain healthy, and it is attempting to find methods of detecting these people. Hospital personnel may carry disease organisms on their hands, another problem to be dealt with by the Department and the Laboratory.

Curing diarrheal diseases is also problematic, as many diarrheal bacteria resist treatment with antibiotics. Isolates of three strains of bacteria are responsible for about half of the cases of acute bacterial diarrhea in Thailand, and these are resistant to most or all available antibiotics. The Department studies the drug susceptibility of all diarrheal bacteria identified, these findings being important to the medical community and as guidelines for stockpiling antibiotics.

Melioidosis

The Department of Bacteriology has begun research in melioidosis, a disease not commonly known but which is thought to be usually fatal. Both man and animals can contract the disease, but the symptoms in man can differ so much from case to case – abscesses, fever, diarrhea, lung involvement, invasion of the bloodstream by the microorganisms – that the disease is hard to diagnose unless blood samples are examined for these bacteria or antibodies. As cultures of this bacteria closely resemble cultures of common, air-borne contaminants, laboratories must be alerted to the possibility of melioidosis so that they will run further tests on cultures which would seem to be of no interest:

Until recently, melioidosis was fatal in 95 per cent of the diagnosed cases because the organism was rarely isolated and then too late for drug therapy to be successful. The disease can be cured with chloramphenicol.

Melioidosis is known primarily in South-East Asia, although it has been found in Australia, and a few cases have been reported in the United States and in South America. The organism has frequently been isolated from soil and water in Malaysia and Viet-Nam and is thought to exist in nature without animal or human hosts.

The Department of Bacteriology is attempting to detect the presence, distribution, and importance of the bacteria which cause melioidosis in Thailand. Water and soil samples are taken, injected into hamsters, and cultures made from the blood of hamsters that die. A few cultures have shown the bacteria of melioidosis.

The Department plans to examine the blood of people in Thailand suffering from undiagnosed diseases, to make serologic surveys in healthy and diseased animals and humans to find antibodies of melioidosis, to investigate how the organism is acquired, and to find the characteristics of resistance. There are also plans to assess the drugs that might be helpful in treatment and to alert medical personnel to both the existence of melioidosis and to proper diagnostic methods.



Dr. A.K.M. Abdul Wahed (left) member of the Technical Committee of the Pakistan-SEATO Cholera Research Laboratory in Dacca, and formerly Director of Health Services for the Government of Pakistan discusses cholera statistics with Dr. Howard E. Noyes at the SEATO Medical Research Laboratory.

Anthrax

The Department of Veterinary Medicine is studying zoonotic diseases, diseases of animals that are transmitted to man. The three being investigated currently are anthrax, leptospirosis, and rabies.

The Department, in its study of anthrax, co-operates with the Department of Livestock Development of the Royal Thai Government and with the Communicable Disease Centre in Atlanta, Georgia. This disease, often fatal in livestock, has a high mortality rate in its human forms. Symptoms of systemic anthrax in man include intestinal involvements and cutaneous lesions, and there is no known prophylaxis, other than prevention and control in animals. Humans may contract the disease by contact with infected animals or by eating raw or under-cooked meat of an infected animal.

To determine the disease's extent and to identify the bacterial strains, soil samples have been taken in all provinces of Thailand in which deaths occurred and the symptomatology has suggested that anthrax was responsible. This information is sent to the Department of Livestock Development, which then attempts to stop the spread of the disease; but control is made difficult by the absence of a regular program of vaccination and by a dearth of veterinary personnel in agricultural areas. Usually an anthrax epidemic is well under way before the news reaches the Laboratory or the Thai authorities. Only then are animals vaccinated.



The Chief of the Department of Veterinary Medicine, Lt. Col. J.H. Morris, tuberculin testing a monkey.

Leptospirosis

Leptospirosis is a second zoonotic disease receiving the attention of the Department of Veterinary Medicine. A bacterial disease having between 95 and 100 strains, it produces abortion in swine; in buffalo lack of appetite, emaciation, and dehydration; nephritis and wasting away in dogs. In man symptoms include malaise, fever, and – in some cases – jaundice, these symptoms persisting for up to three months. Leptospirosis is suspected of being responsible for some of the febrile disorders falling into the category of “fevers of undetermined origin”. There are several diagnostic methods involving serological examination, and the disease can be treated successfully with several antibiotics.

The answer is not complete to the question of how the disease is contracted by animals and man. It is strongly suspected that contact with contaminated water, infected domestic animals, wild rodents, handling of raw infected meat, and eating raw or insufficiently-cooked meat are modes of infection. The Department collects and cultures kidney tissue from cattle, buffalo, and swine brought from all parts of Thailand for slaughter at the Bangkok abattoir and determines the regional incidence and concentration of leptospiral agglutinins.

In addition to the study of domestic animal reservoirs of leptospires, the Department is studying wild animals as possible hosts. Animals are trapped throughout Thailand and are examined to ascertain their role in the transmission of leptospirosis and rabies. This will eventually lead to the classification of the fauna of Thailand.

Water in paddy fields, canals and ponds is also suspect in leptospirosis transmission. Samples are collected and either inoculated into weanling hamsters or are used in direct cultures of rodent kidneys. Hamster and rodent kidneys are minced, cultures made, and isolates obtained and tested.

Control of leptospirosis, like the control of anthrax, is difficult in Thailand. Farmers are largely unaware of methods of and the need for disease control. Also, there is a serious shortage of veterinarians and facilities for livestock diagnosis and treatment.



Bleeding a water buffalo to obtain data for the Department of Veterinary Medicine's study of leptospirosis in North-West Thailand.

Rabies

The Department of Veterinary Medicine is conducting studies of the incidence and distribution of rabies. The large number of stray animals in Bangkok and elsewhere in Thailand makes the problem of rabies control a knotty one, and the incidence of rabies is exceptionally high. In a recent year, there were 50 human cases in Bangkok alone. Control is essential not only for the safety of the people but also because of the substantial yearly loss of farm animals.

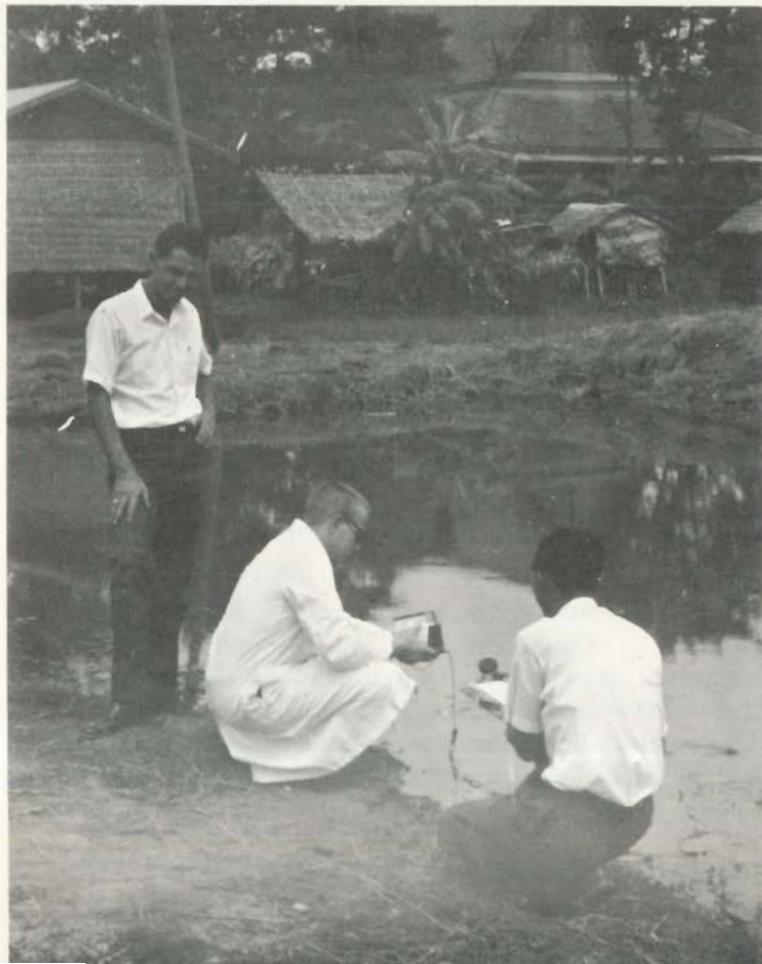
Research workers are investigating and mapping rabies exposure, turning the information over to the Thai Government, which then attempts to halt the spread of the disease.

The Laboratory examines animals that have bitten people, thereby saving a person from a long series of injections if the animal is proven non-rabid.

Development of laboratory animals

The Department of Veterinary Medicine is responsible for the large animal house supplying almost all the Laboratory's and Centre's experimental animals: mice, rats, hamsters, guinea pigs, monkeys, cats, dogs, and rabbits. Aside from its practical role of providing laboratory animals, the Department is trying to improve breeds already in use and to develop other species for laboratory use. In the work of improving animals presently used, the Department is seeking to develop and improve large-scale production methods. Current study is based on mice, rats, guinea pigs, rabbits and hamsters. Primates, cats, and dogs are obtained locally.

Collecting water from a village pond for leptospirosis studies. In centre, Capt. Richard Spertzel, of the Department of Veterinary Medicine.





In the Pathology Department, SP5 Benjamin Woods prepares tissues for microscopic examination.

To develop new species, work is being done with the gibbon and the tree shrew, two primates that could be useful not only to the Laboratory and Centre but for experimentation in other parts of the world. The Department is studying the ecology and biological characteristics of these two animals and is evaluating their usefulness for laboratory work. Research will include study of these animals in their natural habitat, physiological and psychological characteristics under laboratory conditions, reproduction in the laboratory, and disease susceptibility.

The gibbon survives and reproduces in captivity if it is kept in its natural climatic region; however, it is highly susceptible to respiratory infection when taken to another climate. The Department is trying to develop hardier animals and to detail the natural environment of the gibbon so these conditions can be approximated outside the animal's natural climatic region.

The tree shrew withstands climatic change better than the gibbon but has not reproduced in captivity. The development of a domestic breed of this naturally prolific creature is one of the Department's goals.

Nutritional diseases

Work on nutritional diseases of Thailand is being done by the Clinical Research Centre. Several projects have been started and will be expanded.

Anaemia – its aetiology and problems – is being surveyed in Thailand. Anaemia evaluations have been made of families selected at random in central, north-east, north, and south Thailand. Also, several hundred hospital patients in Bangkok have been tested. These investigations include assessment of iron, haemoglobin, vitamin, and enzyme deficiencies. It has been established that anaemia is a vital health problem for Thailand. As a consequence of the leads found during this survey, detailed examinations of the interaction of environmental factors – such as dietary deficiency or excess – with the hereditary forms of anaemia have been studied.

Urinary-tract stones are a problem that has been studied by the Centre for over three years. The Centre has undertaken chemical studies of the disease, which affects as many as 300,000 people in north-east Thailand. Investigations now are aimed at discovery of the cause of bladderstones; diet is a suspected cause, as is dehydration, brought about by the climate or by other maladies, such as diarrheal diseases. When the cause is found, there will be a basis for prevention and treatment.

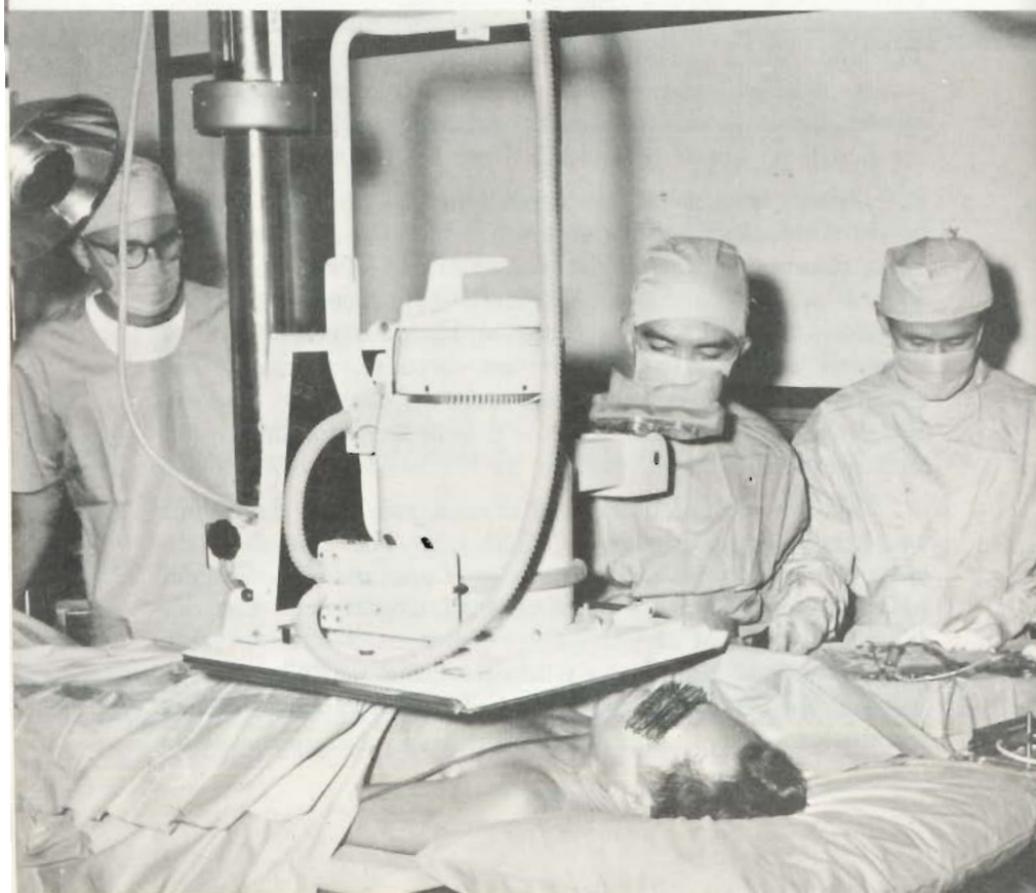
Beri-beri, a third nutritional disease, results in disabilities which are carried through to adulthood. The Centre's study of beri-beri is parallel with its study of anaemia. The disease has been surveyed by evaluating thiamine deficiencies of infants and pregnant and lactating women in comparison with clinical status. The Centre's new facilities will allow continuation and extension of studies of thiamine deficiency and metabolism.

Diseases of the heart

The Clinical Research Centre is making an extensive survey of heart disease among the residents of Bangkok, and a smaller survey is being conducted in the Chiangmai area. Much of this work is carried on in the heart probe and structure laboratory of the Cardiac Catheterization Clinic.

Studies show that heart disease is prevalent among children and adults, and in many cases congenital malformation or rheumatic fever are responsible. In addition to seeking basic facts with which to plan public health programs for prevention, these studies are of immediate value, as they diagnose conditions which can be corrected by surgery already possible in Thailand. Also, the surveys are useful in planning future heart research projects.

Cardiac catheterization team of the Clinical Research Centre make a diagnostic test on a patient.





The Laboratory sponsored a conference on cholera in 1964. The Director of the U.S. Component, Col. James L. Hansen, is shown addressing participants.

Educational Functions

Thailand would benefit much less from the Laboratory's and Centre's research findings and from the presence of modern medical research institutions if they offered no educational services. As Dr. Johnson declared: "A book is worthless unless it is read". So too with medical knowledge and techniques: they must be disseminated to be effective and, therefore, worthwhile.

Lectures, seminars, symposia, and films form one part of the educational program. Topics range from the rudiments of hospital-patient care to scholarly expositions of recent medical research findings. Speakers are recruited from around the world. Students, trainees, and professionals in all phases of medical work are encouraged to attend.

The Laboratory and Centre offer research opportunities for scientists from Thailand and other countries, SEATO members and non-members alike. Here scientists can carry on research significant to South-East Asia and the world,



Scientists take part in a panel discussion on clinical findings at a conference on haemorrhagic fever at the Laboratory. Presiding (at far end of table) is Dr. Aroon Netrasiri, head of the Department of Pediatrics, Siriraj Medical School.

further their education, and learn to use modern equipment and techniques.

Candidates for advanced degrees are doing research at the Laboratory. Not only will their research produce the needed theses, but the students will also have learned a great deal about scientific inquiry, procedure, and reasoning by having worked in a laboratory meeting the highest standards in both equipment and staff.

Many of the technicians employed by the Laboratory and Centre are from Thailand. Here, in the normal course of their activities, they become well-trained in laboratory procedures and techniques. In time a body of fine technicians will be available to the laboratories of hospitals, clinics, and universities of Thailand.

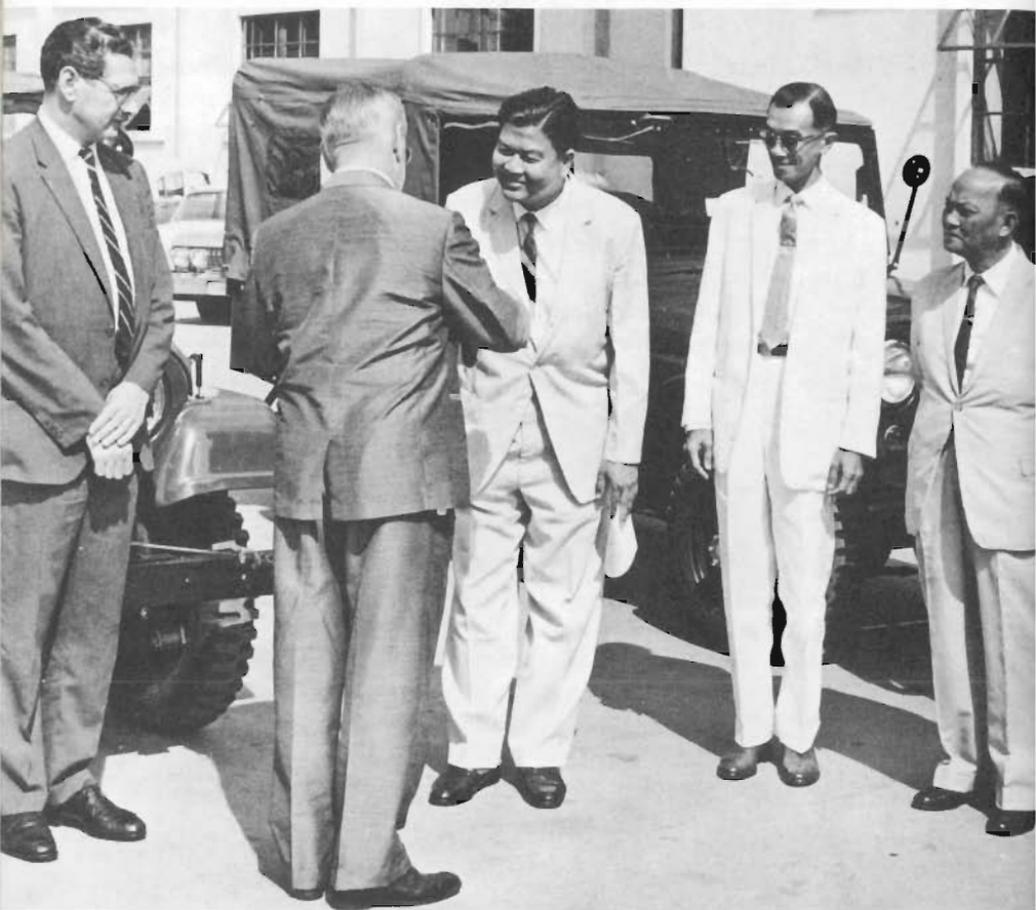
The Future

The Laboratory and Centre plan to expand their educational program. One hope is that professionals, advanced degree candidates, and technicians from a larger number of countries will join the staffs of both institutions.

Current research projects will be continued, and where possible will pass from definition of the problems to determining causes and finding methods of prevention and cure. Research will be extended to include not only other infectious diseases but other medical, surgical, and dental problems of South-East Asia.

“Open house” on SEATO Day, September 8, gives students the opportunity to inspect the work of the Laboratory.





The Deputy Secretary-General of SEATO, Mr. D.A. Wraight (back to camera) hands over to Dr. Swasdi Skulthai, Director-General of the SEATO Clinical Research Centre, the keys of jeeps presented to the Centre by the Australian Government under its program of SEATO assistance. On left is the Australian Ambassador to Thailand, Mr. A.H. Loomes. Others in photo are Professor Jajaval Osathanon, Rector of University of Medical Sciences in Bangkok, and Major-General Pung Pintuyothin, Director-General of the SEATO Medical Research Laboratory.

Glossary of Technical Terms

<i>abattoir</i>	slaughterhouse
<i>aetiological</i>	relating to all factors that contribute to the occurrence of a disease or abnormal condition
<i>agglutinin</i>	any antibody capable of effecting the uniting or adhering of such things as red blood cells, bacteria, virus particles, or rickettsiae
<i>amoebiasis</i>	infection with or disease caused by amoebae
<i>amoeba</i>	single-cell animal widely distributed in fresh and salt water and moist terrestrial situations
<i>antibiotic</i>	a substance produced by a microorganism, such as a bacterium or a fungus, and in dilute solution having the capacity to inhibit growth of or kill another microorganism, such as a disease germ
<i>arthropod</i>	an invertebrate, segmented animal with jointed limbs; includes crustaceans, insects, spiders
<i>bacteria</i>	microscopic plants with single-celled or noncellular bodies, often aggregated into colonies, important to man because of chemical effects and as disease organisms
<i>biopsy</i>	the removal of tissue, cells, or fluids from the living body for examination or study, especially for diagnostic purposes

<i>cardiovascular</i>	of, relating to, or involving the heart and blood vessels
<i>catheterization</i>	insertion of tubular medical device into canals, vessels, passageways, or body cavities so as to permit withdrawal of fluids or substances or to maintain the openness of the passageway
<i>chigger</i>	one of many six-legged larval mites that attach themselves to vertebrates, suck blood, and cause itching and local irritation
<i>cholera</i>	any of several diseases of man and animals usually marked by severe gastrointestinal symptoms
<i>cirrhosis</i>	a chronic progressive disease of the liver or other organs characterized by excessive formation of connective tissue followed by hardening and contraction and that results from unknown cause or from toxæmia, nutritional deficiency, or parasites
<i>congenital</i>	existing at, or dating from birth
<i>conjunctivæ</i>	mucous membrane lining inner surface of eyelids, continuing over forepart of eyeball, and covering corner
<i>cutaneous</i>	of, or relating to, the skin
<i>ecology</i>	a branch of science concerning interrelationships of organisms and their environments
<i>ectoparasite</i>	a parasite that lives on the exterior of its host

<i>elephantiasis</i>	medical condition in which skin takes on appearance of elephant's hide; enlargement and thickening of tissues resulting from obstruction of lymphatics by filarial worms
<i>entomology</i>	zoology that deals with insects
<i>enzyme</i>	a complex substance produced by living cells essential to life by causing chemical transformations in animals and plants
<i>febrile</i>	of, or relating to, fever
<i>flora</i>	plant life
<i>fluorescent microscope</i>	microscope equipped to irradiate material under examination with ultraviolet light in order to detect or study fluorescent components
<i>haemoglobin</i>	an iron-containing protein pigment in red blood cells of vertebrates and functioning primarily in the transport of oxygen from the lungs to the tissues of the body
<i>host</i>	a living animal or plant affording subsistence or lodgment to a parasite
<i>hypotension</i>	abnormally low tension, especially of blood vessels; also called low blood pressure
<i>immunology</i>	a science that deals with the phenomena and causes of immunity
<i>jaundice</i>	yellowing of the skin, occurs with many diseases
<i>lesion</i>	abnormal change in structure of an organ or part due to injury or disease

<i>malaise</i>	a vague sense of physical ill-being
<i>metabolism</i>	the process by which nutritive material is built into living matter
<i>nephritis</i>	acute or chronic inflammation of the kidney affecting its structure
<i>pathology</i>	the study of diseases, their essential nature, causes and development, and structural and functional changes produced by them
<i>primates</i>	mammals, including man, apes, lemurs, generally characterized by binocular vision, appendages for grasping, and enlargement and differentiation of the brain
<i>prophylaxis</i>	the prevention of disease
<i>radioisotope</i>	a radioactive isotope
<i>rain forest</i>	tropical woodland receiving at least 100 in. annual rainfall, usually in a lowland area, and characterized by lofty broad-leaved evergreen tress forming a canopy, vines, and nearly complete absence of low-growing plants
<i>rickettsia</i>	rod-shaped microorganism that lives in cells of biting arthropods
<i>scrub</i>	vegetation consisting chiefly of dwarf or stunted trees and shrubs that is often thick and impenetrable and grows in poor soil or in sand
<i>serological</i>	of, or relating to, science that deals with serums and their reactions and properties
<i>symptomatology</i>	study of disease symptoms
<i>systemic</i>	affecting whole human system

<i>thiamine</i>	member of vitamin B complex essential for conversion of carbohydrate to fat and for normal nervous action
<i>toxin</i>	poisonous substances that are specific products of metabolic activities of living organisms and are typically capable of inducing antibody formation in suitable animals
<i>vaccine</i>	a preparation of killed or living microorganisms administered to produce or increase immunity to a particular disease
<i>vector</i>	a carrier of disease
<i>virology</i>	a branch of science that deals with viruses
<i>virus</i>	a submicroscopic causative agent of infectious disease capable of growth and multiplication only in living cells