

ANNUAL PROGRESS REPORT

SEATO Medic Study No. 94: Studies on the Pathology of Liver Diseases in Thailand: The Role of Dengue Virus in Causing Hepatitis

Project No. 3A 025601 A 811: Military Medical Research Program S. E. Asia

Task 01: Military Medical Research Program S. E. Asia

Subtask 01: Military Medical Research Program SEASIA (Thailand)

Reporting Installation: U.S. Army-SEATO Medical Research Laboratory, APO 146, San Francisco, California

Division of Medical Research Laboratories

Department of Geographic Pathology

Period Covered by Report: 1 April 1963 to 31 March 1964

Principal Investigator: Natth Bhamarapravati, M.D. \*

Associate Investigators: Vikit Teranuvatti, M.D. \*\*  
Uthai Suchinda, M.D.  
Captain Sylvanus W. Nye, USAF, MC  
Praphasri Nimsomburana, M.D.

Reports Control Symbol: MEDDH-28C

Security Classification: UNCLASSIFIED

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## ABSTRACT

SEATO Medic Study No. 94: Studies on the Pathology of Liver Diseases in Thailand: The Role of Dengue Virus in Causing Hepatitis

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The objective of this study is to evaluate the role of dengue virus, if any in causing hepatitis. Patient selection for liver biopsy is being done by the pediatricians and internists of the Siriraj and Vajira

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Hospitals. The laboratory studies being done are: hemogram; coagulation tests; liver function tests; including bilirubin, total protein, electrophoresis and transaminase and antibody titers for leptospira, dengue virus, chikungunya virus and rickettsia. Data from the clinical history, physical findings and hospital course are being recorded on a master sheet for each patient. The program has been in operation for one month and approximately eighteen liver biopsies have been obtained. Immunohistologic study of the tissue has not started. No conclusions can be drawn at this time.

BODY OF REPORT

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Objective: The objective of this study is to attempt to determine whether the dengue virus plays any role in causing hepatitis in Thailand. A review of the pathologic findings in autopsy cases of Thai hemorrhagic fever which

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is caused by dengue virus, has shown that there are lesions in the liver which are somewhat similar to those seen in the early phases of experimental Yellow Fever, thus, it seems likely that the liver may be an important target organ in dengue virus related Hemorrhagic Fever. Other studies by the principal investigator have brought out the fact that in certain rare instances the liver involvement in Thai Hemorrhagic Fever may predominate in the clinical picture and that the patient would then be considered to have viral hepatitis rather than dengue hemorrhagic fever. In this study a correlation with immunofluorescence studies using conjugated dengue antiserum may further clarify this problem.

Description: To accomplish this study a central registry and histopathological laboratory to handle the collection of material, clinical records and laboratory records and processing of tissue has been established at the Siriraj Hospital Pathology Department. The clinical and laboratory data and follow up data are being put on special forms for ready reference. Patient selection for the liver biopsies is being done by the internists and pediatricians of Siriraj and Vajira Hospitals, and the biopsies are being performed by them or their staffs. Serial biopsies accompanied by serial liver function tests are being obtained, circumstances permitting. The blood for laboratory studies is being collected by the staff and the chemical determinations are being done at both Siriraj and the SEATO Medical Research Laboratory.

The appended clinical and laboratory protocol sheet lists the laboratory studies which are being done. Paired sera are being obtained for antibody titers.

To assure that adequate clinical history and significant data from the physical examination and hospital course is obtained, a research fellow and his assistant are visiting the hospitals daily to be sure that the protocols are completed in detail.

It is expected that approximately 500 liver biopsies may be available from Siriraj Hospital and that approximately 250 biopsies may be obtained from Vajira Hospital. In addition, it is planned to study approximately 80 autopsies that are expected annually on patients with liver disease at Siriraj Hospital. Liver biopsy specimens whenever possible, will be fixed for electron microscopy and quenched for immunofluorescent studies. Routinely, hemotoxylin and eosin, iron and reticulum stains will be done. For the analysis, data on each case will be stored in uniform fashion in an indexed case registry. A parallel file will be kept of the microscopic slides and any photographs or other specimens obtained from the patient. The data from these files will be transferred to a punch card system.

Laboratory StudiesBlood

	Date	Value	Date	Value	Date	Value
85. Hg. gm:						
86. JBC:						
87. Diff. P.						
L.						
M.						
E.						
Plasma						
Others						
88. Coagulation time:						
89. Prothrombin time:						
90. Bilirubin :						
direct/indirect:						
91. BSP:						
92. Total protein:						
93. Albumin:						
94. Globulin:						
95. Electrophoresis:						
albumin						
1 globulin						
2 globulin						
globulin						
globulin						
abnormal component						
96. Thymol turbidity:						
97. CCF:						
98. GOT:						
99. GPT:						
100. Alk. phosphatase:						
101. Serum iron:						
102. Cholesterol:						
103. Hb. type:						
104. BUN:						
105. NPN:						
106. FBS:						
107. G6PD deficiency:						
108. Reticulocyte count:						
109. Nucleated red cells:						
110. Platelet:						
111. L3 cells:						
112. Iodine test:						
113. Leptospirosis ab.						
114. Dengue:						
115. Chikungunya:						
116. Rickettsial:						
117. Antibody (other) :						
118. Vitamin A:						
119. Vitamin B:						
120. Vitamin E:						
121. Malaria smear:						

Progress: The project has been functioning for one month and approximately 18 liver biopsies have been obtained in this period. Sera from these patients have been stored in a minus 85°C freezer until the Biochemistry laboratories at the SEATO Laboratory are fully functional. Immunohistologic study of the tissue has not been started.

Summary and Conclusions: No conclusions are possible at this time