FINAL PROGRESS REPORT

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Submitted by

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1. Clinical studies of cases exposed to anticholinesterase agents at the Rocky Mountain Arsenal have been completed. One article was published on the results of this work. See attached reprint. The remainder of the data is being prepared for publication and will include approximately 1000 cases of exposure to these agents. The final article will be forwarded when completed.

2. A study of changes in blood coagulation following exposure to anticholinesterase agents was completed and the data was recently published (von Kaulla, Kurt and Holmes, J.H. Changes following anticholinesterase exposures, Arch. Environ. Health, 2: 168, 1961).

3. Studies were made of persons exposed to anticholinesterase agents on an accidental basis in the Colorado area, the majority representing those working with such insecticides as parathion, TEPP, and phosdrin. This study was a voluntary program based on contacts with the physician or those working with these insecticides in the Colorado area. It also served to demonstrate the public aspects of this problem. A case report of a severe parathion poisoning was presented in the Rocky Mountain Medical Journal, 54: 1022, 1957. An article for persons working with these insecticides was published in a national florist magazine (Holmes, J.H. Some medical comments relating to handling insecticides. Florists' Review, CXXVII, No. 3290: 21, 1960).

A complete report including blood studies and clinical observations among exposed workers covering 7 years (1955-61) is currently being prepared for publication. This will be forwarded when complete.

4. A series of patients with glaucoma who were being treated with phospholine iodide (anticholinesterase agent) were studied over a prolonged time period to determine the chronic systemic effects resulting from prolonged eye drop administration. Glaucoma patients being treated by other methods served as a control group. This is currently being written up and the final report will be forwarded when completed.

5. Data on EEG changes observed following anticholinesterase exposures is currently being reviewed in the Department of Psychiatry and a final report will be submitted when the work is completed.

6. The results of the psychological testing, the psychiatric interviews, and long-term follow-up studies have been presented in Progress Reports but never compiled as a unit. In view of a recent article in Lancet regarding the psychiatric effects of these agents it seems pertinent to compile the available information in a final form. This is being done and will be forwarded when completed.

7. Clinical observations on the use of 2-PAM in treatment of anticholinesterase exposures will be compiled and forwarded when complete.

8a. Studies were made of the red cell cholinesterase concentration in various types of anemia and blood dyscrasias and the completed report has already been forwarded.

8b. Studies were made of the changes in the plasma cholinesterase concentration in various types of renal disease, in patients with hypoproteinemia and in patients with liver disease. The test may prove diagnostically valuable in assessing hepatic damage in certain

types of renal disease. A final report will be forwarded when completed.

Basic work done under this contract included the following projects:

9. Studies were made of the effect of administration of atropine in normal persons on blood composition, renal function and salivary flow. Report has been submitted.

10. Studies of the effect of anticholinesterase agents on the rate of passage of Na_{24} across the blood brain barrier were completed, and a summary of the data was submitted in a Progress Report. This data indicated that neither physostigmine nor atropine altered significantly the rate of passage of Na_{24} across the blood brain barrier in rats and rabbits over the four-hour period studied.

Measurements were made of the changes in plasma and extracellular volume produced by injection of physostigmine and acetylcholine and of the blocking effect of atropine. The essential data was presented in a previous Progress Report.

In vitro studies were done on changes in rate of transfer of radio-active isotopes across the red cell membrane after inhibition of red cell cholinesterase activity by anticholinesterase agents. This also included studies of the effects of blood storage on the red cell and plasma cholinesterase activity. Preliminary reports of the results were submitted.

Studies were also made of the changes in liver blood flow and BSP clearance produced by injection of physostigmine and acetylcholine in the unanesthetized dog. Additional experiments were performed in which atropine was administered prior to injection of physostigmine. A brief summary of the results of these experiments is being forwarded.