

## Medical Research at Dalhousie

### Article 4. — Department of Pharmacology

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The period between 1949 and 1951 marked a turning point in the research activities of the department of Pharmacology. Prior to this time research had been carried on by the one, and later two men who comprised the staff. The appointment of a third full-time man to the staff in 1951 together with the inauguration of a program of graduate training in Pharmacology during the 1949-50 session, set the scene for a greatly accelerated research activity.

At the present time each member of the staff is carrying on his own independent research program. Work which could be classified broadly as toxicological is being directed by Dr. J. G. Aldous, and two problems are currently being investigated. One, which receives financial support from the Defence Research Board, is concerned with the mechanism of action of cytotoxic agents, some of which are potentially useful in chemical warfare. A somewhat unique approach to the problem is used here in that the usual techniques of testing the sensitivity of intracellular extracts toward the agent in question has been abandoned in favor of treatment of the living cell with the agent and then performing enzymatic assays on the intracellular extracts. The information derived from such a study then relates directly to the action of the chemical agent upon enzymes inside the cell rather than

upon extracts from the cell whose physical state and therefore affinity for the toxic agent may be altered by the extraction procedures. During the last 8 years this program has covered a variety of cytotoxic agents including iodoacetic acid, ultraviolet and X-ray radiations, mustard gas and nitrogen mustard.

The second program, financed by a grant from the National Research Council, has as its objective, the design of a more satisfactory method for assaying toxicity of local anesthetics than is currently employed. These drugs are rapidly metabolized in the body and this fact is being used as a basis for an expression of toxicity. It is of interest to note that this program originated as the result of co-operative effort with the Department of Anesthesia, to provide basic science requirements for a specialty in Anesthesia, and illustrates how a program of this type can be of benefit to both parties.

Dr. A. K. Reynolds, assistant professor, has directed his activities along two lines. For several years he has been preparing a monograph entitled "Morphine and Allied Drugs." Dr. L. O. Randall, Hoffman-LaRoche Ltd., is the co-author of this comprehensive treatise which covers the work of 1600 authors in the field. The monograph will be published shortly by the University of Toronto Press.

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More recently, Dr. Reynolds has been working on an N.R.C. financed project which is concerned with the pharmacodynamics of some new alkaloids of Rauwolfia.

Investigations into the mechanism whereby tolerance is developed to morphine and related narcotics is under the direction of Dr. J. C. Szerb, assistant professor. This project is financed jointly through the N. R. C. and Hoffmann-LaRoche Ltd. This problem which for many years has challenged the imagination of research workers, has been hampered by the lack of a method sufficiently sensitive for the quantitative detection of therapeutic concentrations of morphine in body tissues. After almost two years, Dr. Szerb, assisted by his graduate students, has succeeded in formulating a method which will detect as little as 3 micrograms of morphine per gram of tissue. The method has already been applied to the question of whether or not the distribution of morphine in the central nervous system differs in tolerant and non-tolerant animals.

From time to time the department has embarked on research programs with other departments. The mechanism of action involved in acute methyl alcohol poisoning has been investigated jointly with the Department of Medicine, while the identification of the hyperglycemic factor of urine has been the object of a study originating in the Department of Metabolism, Victoria General Hospital. Assistance was also given the Department of Psychology in designing experiments to test the effect of chlorpromazine on the ability to perform certain personality tests.

The training program for research in Pharmacology which has been in operation since 1951 is somewhat unique in Canada. During the 1954-55 session, four candidates for the M. Sc. degree were enrolled, three of whom have since graduated. Two of these graduates are presently pursuing studies leading to the Ph.D. at other Canadian Universities. As an indication of the academic attainments of these graduate students, three scholarships of the Faculty of Graduate Studies at Dalhousie were awarded to this department during the period 1953-55.

In summary, the research activities of the Pharmacology department are directed not only toward performing research, but also to provide the training for research workers.

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