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This Symposium was organized by the Clinical Research Institute of Montreal under the auspices of the University of Montreal Medical School

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The Clinical Research Institute of Montreal

Preface

The Clinical Research Institute of Montreal, inaugurated in April 1967, introduced a new concept of organization of clinical research in teaching medical centers. Adjacent to the Hôtel-Dieu Hospital, a major teaching hospital of the University of Montreal, the "professional" or career clinical investigators were grouped under one roof with common auditorium, seminar rooms, instruments rooms, cold rooms, experimental surgical rooms and illustration department, with administration, accounting division and machine shops at the service of the research workers.

Besides its large multidisciplinary team working on various aspects of hypertension, the Institute includes research teams in the following fields: 1) neurobiology and Parkinson's disease, 2) lipids and atherosclerosis, 3) molecular biology, 4) immunochemistry, 5) pituitary polypeptides and proteins, 6) nutrition and 7) clinical pharmacology of new drugs.

Research is financed entirely by grants obtained from accredited agencies, mostly from the Medical Research Council of Canada. These grant monies constitute about 50% of the entire budget of the Institute while the other half for administration, maintenance and physical facilities is financed through the support of the Ministry of Social Affairs of Quebec.

The grouping of full-time clinical investigators in various fields under a single roof has facilitated the exchange of ideas, has initiated many joint projects and has greatly encouraged collaboration at all levels. This has resulted in a high degree of harmony, unity and happiness in work which are rarely seen. All research projects must have a direct relationship to clinical problems and may involve work at any level, be it at the fundamental or clinical level, be it biochemical, histological, physiological, experimental or clinical pharmacology. They necessitate the same type of sophisticated and advanced electronic equipment as seen in any basic laboratories, including gas chromatography, amino-acid analyzers, sequencer, electron microscope and others. The planning of the Institute has produced an economically simple but highly effective structure that can readily be adapted to the needs of any research worker or project.

Because of its position, the Clinical Research Institute plays an important part as a bridge between the French and English medical centers of Canada's metropole. As an example, the Clinical Research Institute has organized an advanced course on Cellular Biology recognized for advanced postgraduate training by the Department of Experimental Medicine of McGill University and the Department of Medicine of the University of Montreal, with half of the teachers coming each from the anglophone and the francophone universities.

The aims of the Institute are to advance our knowledge of normal and abnormal physiopathology and diseases, to train teachers-scientists and research workers and to bring a climate of excellence in the community it serves.

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Contents

Introduction

J. GENEST

Our first Symposium on Hypertension was held in Ste Adèle-en-Haut, Que., in October 1963 and its Proceedings were published in less than three and a half months, that is in January 1964, as a special issue of the Canadian Medical Association Journal. It soon became a standard source of reference for all research workers in the field of the renin-angiotensin-sodium aspects of hypertension. This meeting coincided with major advances in the field, in new methods for measuring plasma renin activity, in the demonstration of the relationship of the renin-angiotensin system to sodium regulation and of the relationship of renin-angiotensin, aldosterone and sodium in clinical and experimental hypertension.

We have been fortunate in the organization of this second Symposium to have most of the participants of the first Symposium and many other scientists who have contributed significantly to the field since 1963. This second Symposium deals with important new advances concerning tissue renins, angiotensin I converting enzyme activity, new radioimmunoassay methods for the measurement of angiotensin I and angiotensin II, the control of the renin secretion and release, the disturbance of aldosterone regulation in early, uncomplicated benign essential hypertension and the 18-hydroxydeoxy-corticosterone secretion rate in early hypertension. As for the first Symposium, this second one has been entirely funded from Canadian sources. We are glad to express our gratitude to the Ministry of Social Affairs of the Province of Quebec, to the Medical Research Councils of Canada and of Quebec, to the Department of National Health and Welfare of Ottawa and to the Dean of the University of Montreal Medical School, Dr. Pierre Bois, for their active and generous support.

We are proud to say that we did not ask for any financial support from American sources for we are convinced that their ready understanding of the necessity of such symposia has become an excuse for scientists in many wealthy western countries to dispense with the efforts needed to convince their own governments and their research agencies of the importance of adequate financial support of medical research and of such scientific symposia and meetings. We have the greatest admiration for the American generosity in the scientific and medical fields but this cannot be taken as an excuse for inertia for many scientists for not exerting in their own countries, sufficient pressure for greater support for medical research and related activities.

We have done away with the recording of the discussions which delay publication of Proceedings for periods of 9–15 months. Instead, the discussions after each paper were summarized in a critical way by an expert in the field. These summaries are added in the Proceedings. The value of such a Symposium for all those inter-

ested in the field has its importance only if those who could not be invited because of space and budget limitations, have rapid access to the new information presented. Hence, the decision for the solution adopted, the Editorial Board verifying that all manuscripts conform to the regulations and every participant being responsible for the quality of style and presentation of his own paper.
We hope that this Symposium will serve as those in the past to strengthen the friendships between the many research workers in the field and facilitate and encourage exchange of ideas.

The Remarkable Story of Hypertension

IRVINE H. PAGE

To introduce such a superb program it is well that in the name of the audience I thank Dr. Genest and his associates who over the years have continued to show not only great scientific productivity but great organizing ability as well. I know God created the earth in six days without the help of a committee; the amazing thing is that Genest created a conference with a committee!
I must not set a bad example by exceeding my time limits. I might as well give you an outline of the story of hypertension in five minutes as in five hours. I am not sure where it will take as but at least we will go there faster.
Not so long ago hypertension was considered a good thing because it compensated for the narrow blood vessels adequately to perfuse the tissues. We would all have starved then. The age of amateur quackery was concurrent, when D'Arsonvalization, potassium iodide, purges, red meat, garlic and even "whiffles" garlic were prescribed. Later came those like rutin, nephritin and probably huge doses of vitamin C. It was an era which like the poorly endowed woman with the sequined sweater, was much ado about nothing.
The age of mechanism was ushered in by production of X-ray nephritis, surgical reduction of renal parenchyma, but nothing truly reliable until the clamp on the renal artery was introduced. It was then shown in hypertensive patients that arterial pressure could be reduced without reduction in tissue perfusion and the way was thus open for effective treatment. The neurological, chemical and hemodynamic mechanisms have since provided all of us with tenure. It gradually dawned that hypertension was a many splendored thing and not a single entity with a single cause; a "mosaic" if you will.
The age of surgery was a natural progression with sympathectomy leading the van followed by nephrectomy, adrenalectomy and renal artery repair. Times were more peaceful then and the Roman Circus had not been introduced, so we medical men could live with the surgeons. In those days they could not resurrect our medical failures by a heart transplant to give a few months of life!
And then came the age of the Pill. You remember the unfortunate woman who forgot to take her pill and got into trouble because she was practicing license without a medicine. I need not detail the enormously valuable remedies that in