

HYPERTENSION

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Preface

In 1952, we set up a Clinical Research Department at the University of Montreal Hôtel-Dieu Hospital which was devoted to the study of the basic mechanisms of human hypertension as related to the hormonal-metabolic factors thought to be involved in the increased peripheral resistance. On two occasions, in 1963 and 1971, during periods of major advances, we organized international symposia, the first at Chantecler Hotel, Ste Adele, Que., and the second at the Mont-Gabriel Lodge, Mont-Gabriel, Que. Their proceedings were rapidly published, the first one within three months (*Canadian Medical Association Journal*, vol. 90, January 1964), and the second one within six months as a book entitled *Hypertension '72* by Springer-Verlag.

These two publications served as reference sources for all those interested in the various aspects of hypertensive cardiovascular diseases. The research productivity of our Multidisciplinary Research Group was officially recognized by the Medical Research Council of Canada by a Group Grant Award in 1972.

Instead of a third international symposium on the occasion of the 25th anniversary of our Research Institute in 1977, we have felt that a more significant contribution could be made by editing an international textbook on hypertension, especially prepared for practicing physicians, medical students and all those interested in the various aspects of experimental and clinical hypertensive diseases. The resulting volume is *HYPERTENSION: PHYSIOPATHOLOGY AND TREATMENT*. The list of contributors includes many of the leading experts, researchers, and specialists in the field from more than twelve countries.* Such a textbook arrives, we feel, at a very opportune time when the medical profession, society in general, and governments of many nations have begun to realize that hypertension is one of the most important and prevalent diseases facing mankind, that it can be easily detected and adequately controlled with the

available medication. Recent findings from many centers have demonstrated that severe cardiovascular complications, which are the most frequent causes of morbidity and mortality in the Western world, can be prevented.

By giving to the medical profession an up-to-date and authoritative textbook on the whole subject of hypertensive cardiovascular diseases, it is our hope that hypertension will be better understood by practitioners of medicine and that the patients will be better treated and will more closely comply with the therapeutic regimen prescribed.

This book covers experimental as well as clinical hypertension from the point of view both of mechanisms and of management. In Part Two the chapters on the physiopathology of the various hypertensive cardiovascular diseases examine in depth the participation of hemodynamic factors, the central nervous system, the autonomic nervous system, the renin-angiotensin system, adrenocortical hormones, kinins, prostaglandins, arterial contractility and reactivity, and the role of cations. In Part Three the various aspects of human hypertensive diseases are covered: epidemiological factors, investigation of the hypertensive patient, personality and emotional factors, and the target organs responsible for the hypertensive cardiovascular complications—brain, eye, kidney, and heart. The various types of secondary hypertension are described in detail: primary aldosteronism, pheochromocytoma, contraceptive pill hypertension, Cushing's syndrome, coarctation of the aorta, adrenal enzymatic defects, acromegaly. Special attention has been devoted to the management and treatment of essential hypertension and to the pharmacology of antihypertensive drugs. Because atherosclerosis is an integral part of, and greatly accelerated by, hypertension, its pathogenesis, biochemical pathology, and histopathology are examined in the light of the most recent findings.

The various types of experimental hypertension and the physiopathological aspects of spontaneous hypertension in rats are covered in sufficient detail to bring the pertinent information to the practitioners and all those interested in the general field of hypertension. For more detailed information, the lists of references are sufficiently large to permit the reader to go to the original data or to more extensive reviews of given aspects to obtain more information on small but important points.

To give the reader a balanced view of the management and treatment of hypertension, we have been fortunate to have three of the world experts in this field: one from United States, Dr. James C. Hunt who has had extensive clinical experience; and two from Great Britain, Dr. Colin Dollery, well known for his

*We would like to pay a special tribute to Dr. Lewis K. Dahl from Brookhaven National Laboratories, a friend of many years, who gave us his manuscript while in the terminal phase of his fatal illness, as a sort of scientific testament. We want to acknowledge our debt of gratitude and admiration to Dr. Dahl, who has contributed so much to one of the most basic facets of hypertension and whose work, while neglected or downgraded in its early phase, has now been recognized as of fundamental importance.

clinical pharmacological studies in this field, and Dr. Brian Prichard who has been the leader in the use of β -blocking drugs. The reader will become better acquainted with some of the antihypertensive agents used in Great Britain and in Europe, but not yet on the market in North America, and will also see the differences in approach from which he can derive his own conclusion in relation to any particular case. In addition, we have asked leaders in the field who have spent a lifetime of research work into the mechanisms of hypertension to give their personal views on the fundamental mechanisms of hypertension. They include: Sir George Pickering, Dr. Irvine Page, Dr. William Stanley Peart, Dr. Louis Tobian, Dr. Arthur Guyton, the Glasgow group of Dr. Anthony F. Lever, Dr. Jehoiada J. Brown and Dr. J. Ian S. Robertson, the late Dr. Lewis K. Dahl, and our group in Montreal. In this way, we believe that the reader will be more enlightened as to both the differences and the similarities between key investigators and the difficulties that they encounter in their quest for a better understanding of the disease.

We wish to acknowledge the invaluable help and guidance received from the editorial staff of McGraw-Hill in the preparation of this textbook. We also want to mention particularly the unfailing and generous collaboration of our secretaries: Lise Lanthier, Lucette Major, Anne Haché, Anne Masseau, Linda Paquette, and Carole Tremblay, who brought most competent secretarial expertise to the preparation of this book. We are also grateful to Miss Isabelle Morin and Mr. Oswald Taliana for the redrawing and photographing of many figures and to Mrs. Lorraine Biemann and Françoise Julien, our librarians, for correcting the galley proofs. We wish finally to express our debt of gratitude to our wives for their support and understanding during the preparation of this textbook.

On the occasion of this 25th anniversary of our research group, it is our most sincere hope that this book will serve effectively to advance our attempts to help those suffering from hypertensive cardiovascular diseases and their complications.

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To give the reader a balanced view of the management and treatment of hypertension, we have been fortunate to have three of the world experts in this field: one from United States, Dr. James C. Hammon, who has had extensive clinical experience, and two from Great Britain, Dr. Colin Doherty, well known for his

textbook, and Dr. David S. Gann, who has been a pioneer in the field of hypertension. We feel that a very appropriate time when the medical profession, society in general, and governments of many nations have begun to realize that hypertension is one of the most important and prevalent diseases facing mankind, that it can be easily detected and adequately controlled with the

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PART ONE *Introduction*

Generalities on hypertension

WILLIAM STANLEY PEART

The first approach to a definition of arterial hypertension has to be through its measurement, and one of the most important considerations has to be the apparatus and the circumstances of such measurement.

Measurement of arterial pressure

The standard instrument, of course, is the ordinary mercury type of manometer. It must be considered superior to the aneroid variety, which should not in general be used because of its need for frequent calibration.

The size of the cuff is of great importance, and although this has not been very well standardized for all ages (see Robinow et al. [1] on children), the original standard of von Recklinghausen [2] seems best. For an adult the width of the cuff should be about two-thirds of the length of the upper arm, which means about 13 cm wide and 30 cm long. Cuffs which are too narrow lead to elevated blood pressure measurements. In order to obtain reproducible values, the arm of the patient must be relaxed. Many patients instinctively contract their fist and arm muscles when the cuff is inflated, and they must be positively told to relax the arm since such contraction is known to increase the arterial pressure reflexly. In fact, isometric contraction is one of the more potent pressor stimuli [3].

The rate of inflating the cuff is of less importance than the rate of deflation (see Rosé and Blackburn [4] for critical discussion). The heart rate is very important in relation to the rate of deflation since at slow rates it is impossible to make large errors if the mercury is allowed to fall too rapidly; for example, a rate of fall of 10 mmHg per second at a heart rate of 60 can easily lead to an error of 10 mmHg for that factor alone. The end points used by most physicians and agreed by international convention are the appearance of the Korotkov sounds at systolic pressure and the point of muffling. Although previously there was considerable doubt, it is now universally agreed that this is the point which is most closely correlated with direct measurement of diastolic pressure [5]. There are still many who in practice record the point of disappearance. This is sometimes close to the point of

muffling and sometimes 20 mmHg or more away from it, and of course in some patients with wide amplitude pulses (fever, aortic incompetence, and anemia), the sounds can be heard right down to zero.

There are a number of problems in such a seemingly simple process. The silent gap is very important since it leads the inexperienced to record too low a systolic and too high a diastolic pressure. As the cuff pressure is lowered, the sounds disappear, sometimes with a preliminary muffling, and then reappear to undergo the ordinary muffling at the true diastolic pressure. This phenomenon is seen in patients with high blood pressure; the solution is, of course, to palpate the artery during cuff inflation to estimate systolic pressure and to listen down to at least 100 mmHg on deflation of the cuff. The phenomenon of the disappearing sounds is very strange, and there are many patients in whom the sounds disappear completely so that neither systolic nor diastolic pressure can be heard usually after the first reading. One solution is to take the blood pressure in the opposite arm; the other is to wait for a few minutes, when the sounds may often be readily heard once more. It is important to recognize that this phenomenon may affect the artery halfway through the process of taking the blood pressure so that the sounds fade away somewhere between the systolic and the true diastolic pressure. It should be suspected if there is no transition from a harder note to a softer note which enables the muffling point to be recognized with ease in most subjects. There should be no compulsion to record a diastolic pressure for the sake of a figure. Since this phenomenon is quite common in patients treated with various drugs, a doubt should be recorded, as this is the truth of the matter. The phenomenon is rather puzzling since the radial pulse may be felt pulsating equally well whether the sounds can be heard or not.

The next problem for the observer concerns the variation in his or her observations [4,6]. This was first emphasized in the rate of deflation of the cuff, but equally important is digit preference. It has been shown that many people prefer numbers ending in 0 or 5 to even numbers such as 4 or 8. Depending on the rate of fall of the mercury and the particular digit preference, quite a large error can creep into individual measurements. Although this is not commonly done, it might be better for an observer to state that the reading is to the nearest 5 or 10. This becomes rather important when considering diastolic pressure.

The next observer problem is that of previous knowledge of the blood pressure and what the observer may wish the pressure to be. This sort of bias is particularly important in drug trials but also enters into insurance examinations or examinations in situations where the patient's job may depend upon the answer. This self-deception, which is not really in the interests of the patient in the long term, may even