Cardiovascular Clinics

VOLUME TWO | NUMBER THREE

International Cardiology

Paul Dudley White, M.D. | Guest Editor

VOLUME TWO | NUMBER THREE

International Cardiology

Paul Dudley White, M.D. | Guest Editor

F. A. DAVIS COMPANY, PHILADELPHIA

 Library of Congress Catalog Card Number 74–139333
ISBN 0–8036–9270–6

Cardiovascular Clinics Series:

1 | 1 Hypertensive Cardiovascular Disease
1 | 2 Coronary Heart Disease
1 | 3 Cardiovascular Therapy
2 | 1 Congenital Heart Disease
2 | 2 Arrhythmias
2 | 3 International Cardiology

Editor's Commentary

The physicians of the world constitute an international fraternity linked by a common goal, i.e. the search for scientific information which can be used to prevent or treat disease. The universality of our scientific efforts is nowhere more evident than in the subspecialty category of cardiology. Monumental contributions have been made in the past by such international greats as William Harvey (anatomy of the heart), Stephen Hales (hydraulics of the blood and blood vessels), John Baptist Morgagni (valvular heart disease), William Heberden (angina pectoris), William Withering (digitalis), Rene Laennec (auscultation), Robert Adams and William Stokes (Adams-Stokes syndrome), Austin Flint and Graham Steell (cardiac murmurs), Heinrich Quincke (capillary and venous pulse), Wilhelm His (atrioventricular bundle), Willem Einthoven (electrocardiography), and Sir William Osler (infectious endocarditis), among others. The present issue of CARDIOVASCULAR CLINICS provides an opportunity for clinicians, especially in the United States, to reflect on the many important contributions being made currently by our colleagues from around the world. No single physician in our time has contributed more to the understanding of cardiovascular disease than has Paul Dudley White. I am forever grateful to Doctor White for the effort expended in assembling this issue.

ALBERT N. BREST, M.D.

Contributors

A. Alvarado-Toro, M.D.
Fellow, Institute of Cardiology, Mexico City, Mexico

Christ Aravanis, M.D.
Associate Professor of Cardiology, Program Director for the Study of Coronary Heart Disease, Department of Cardiology, University of Athens Medical School, Athens, Greece

Klaus D. Bock, M.D.
Professor of Medicine and Head of the Division for Renal and Hypertensive Diseases, Klinikum Essen der Ruhruniversitaet, Federal Republic of Germany

Jan Brod, M.D.
Professor of Medicine, Medical School Hannover, Federal Republic of Germany

F. Perez Casar, M.D.
Department of Cardiology, General Pathology Service, Prof. A. Fernández Cruz School of Medicine, University of Madrid, Madrid, Spain

Yves Castonguay, M.D.
Staff Surgeon, Montreal Heart Institute, Montreal, Canada

Marcelo V. Elizari, M.D.
Chief, Department of Electrocardiography, Hospital Argerich, Buenos Aires, Argentina

J. Espino-Vela, M.D.
Head, Department of Pediatric Cardiology, Institute of Cardiology, and Professor of Medicine, University of Mexico, Mexico City, Mexico

Claude M. Grondin, M.D.
Staff Surgeon, Montreal Heart Institute, Montreal, Canada

Pierre Grondin, M.D.
Chief, Department of Surgery, Montreal Heart Institute, Montreal, Canada

M. Susana Halpern, M.D.
Member, Department of Electrocardiography, Hospital Argerich, Buenos Aires, Argentina

Julio O. Lázzari, M.D.
Member, Department of Electrocardiography, Hospital Argerich, Buenos Aires, Argentina

Gilles Lepage, M.D.
Senior Staff Surgeon, Montreal Heart Institute, Montreal, Canada

Pavel Lukl, M.D.
Professor of Medicine, Head of Ist Medical Clinic; President of the European Society of Cardiology, Olomouc, Czechoslovakia

Kempson Maddox, M.D.
Consulting Physician, Royal Prince Alfred Hospital and Royal Hospital for Women; President of the International Society of Cardiology, Sydney, Australia

Claude Meere, M.D.
Staff Surgeon, Montreal Heart Institute, Montreal, Canada

Alessandro Menotti, M.D.
Research Assistant, Centro per le Malattie Cardiovascolari, Dipartimento di Cardiologia, Ospedale San Camillo, Rome, Italy

Blas Moia, M.D.
Associate Professor of Medicine, Buenos Aires University; Chief, Institute of Cardiology, Ramos Mejia Hospital, Buenos Aires, Argentina

Risteárd Mulcahy, M.D.
Director, Cardiac Department and Coronary Care Unit, and Director, Coronary Heart Disease Research Unit, St. Vincent's Hospital; Staff Member, Departments of Internal Medicine and of Social and Preventive Medicine, University College; President, Irish Medical Association and the Irish Heart Foundation, Dublin, Ireland

Gerardo J. Nau, M.D.
Member, Department of Electrocardiography, Hospital Argerich, Buenos Aires, Argentina

Henry N. Neufeld, M.D.
Professor of Medicine and Chief, Heart Institute, Tel-Hashomer Government Hospital, Tel-Aviv University Medical School, Tel-Aviv, Israel

S. Padmavati, M.D.
Senior Consultant in Cardiology, G. B. Pant Hospital;
Professor of Medicine (Cardiology), M. A. Medical College, New Delhi, India

Vittorio Puddu, M.D.
Director, Centro per le Malattie Cardiovascolari, and Primario, Divisione Cardiologica B,
Dipartimento di Cardiologia, Ospedale San Camillo, Rome, Italy

Francois C. Reubi, M.D.
Professor of Medicine and Director, Medical Outpatient Department,
University of Berne, Berne, Switzerland

Mauricio B. Rosenbaum, M.D.
Chief, Service of Cardiology, Hospital Salaberry, Buenos Aires, Argentina

V. Schrire, M.D., Ph.D.
Associate Professor of Medicine, University of Cape Town,
Cape Town, South Africa

F. O. Simpson, M.B.
Associate Professor of Medicine, University of Otago Medical School,
Dunedin, New Zealand

F. Vega Diaz, M.D.
Member, Spanish Society of Cardiology, Madrid, Spain

Zeev Vlodaver, M.D.
Research Associate and Cardiologist, Heart Institute, Tel-Hashomer Government Hospital,
Tel-Aviv University Medical School, Tel-Aviv, Israel

Paul Dudley White, M.D.
Emeritus Clinical Professor of Medicine, Harvard Medical School,
Boston, Massachusetts

Contents

Prologue

Cardiovascular Clinics is fortunate to have such a wealth of material about various aspects of all kinds of heart disease presented by authorities from every continent of the world, many of them pioneers in their own lands. It has been my good fortune to have known most of the authors or their masters personally as old friends when we pioneered together, sometimes along the same advances in clinical cardiology and sometimes hand in hand. Although, as to be expected, for reasons of language and concentration of experience, more contributions come from Europe than from any other continent, much of new interest in cardiology has come from every corner of the globe; and certainly peoples outside the confines of the Old World of Europe and the New World of the U. S. A. will be heard from increasingly in the future. It would be of interest to note the Table of Contents of such an issue as this, in the year 2000 A. D., when the contributions from the "rest of the world" could easily outnumber those from Europe and the U. S. A. The current pioneering of Padmavati of Asia on Cor Pulmonale, of Schrire of Africa on Cardiac Transplantation, and of Maddox of Australia on Presenile Coronary Heart Disease is proof of the far-flung talent in medical science.

It also interests me that although coronary heart disease, hypertension, and cardiovascular surgery easily and justifiably hold the limelight in the U. S. A. today, such important though often neglected subjects as the cardiac neuroses and the relationship of stress and physical labor to heart disease are included in this relatively small number of articles. It is, I am sure, the hope of many of us interested in the role of medical science internationally as a most important tool in the advance of cardiology and thereby in the better understanding and the formation of peace throughout the world, that future issues of this nature will be stimulated by this tentative but auspicious beginning.

PAUL DUDLEY WHITE, M.D.

Hypertensive Heart Disease

Klaus D. Bock, M.D.

According to the Health Examination Survey[1] 17 million (or 15.3 per cent) of the adult North American population have definite hypertension, and 10.5 million (or 9.5 per cent) have definite signs of hypertensive heart disease. These figures not only indicate the great importance of hypertension and its complications for the health of the nation but also reveal, in accordance with many other published works, that about two thirds of hypertensive patients have cardiac manifestations of their disease. Furthermore, the most frequent causes of death in untreated hypertensives (30 to 80 per cent[2,3,4]) are cardiac in origin.

The heart disease of the hypertensive patient originates from two different pathogenetic mechanisms occasionally operating separately but usually occurring together. One is the increased work load of the heart, at first causing hypertrophy, later dilatation and failure of the left ventricle. The other is coronary vascular disease, mainly due to arteriosclerosis. The etiology of coronary arteriosclerosis is multifactorial; often it is found without any elevation of blood pressure, but it occurs more frequently in hypertensive than in normotensive animals[5] and human beings.[6,7,8,9] These two pathogenetic mechanisms ultimately determine the nature of the cardiac causes of death in hypertensive patients, namely, left ventricular failure, congestive heart failure and myocardial infarction.

The following discussion refers to hypertensive heart disease in primary and secondary hypertension uncomplicated by such factors as azotemia, anemia or electrolyte disturbances which may have additional adverse effects on the heart.

CARDIAC HEMODYNAMICS IN HYPERTENSION

In the absence of heart failure patients with established essential hypertension have a normal cardiac output and increased peripheral resistance.[10–14] The heart rate is normal or only slightly elevated, resulting in a normal stroke volume. However, young patients or those in the early stage of the disease may have a high cardiac output, an elevated heart rate, a normal stroke volume and a normal peripheral resistance.[15–18] Compared with essential hypertension the cardiac output in renovascular hypertension is slightly elevated.[19] Other forms of renal hypertension show variable changes of the cardiac index, depending on the type and the stage of the underlying disease; however, the peripheral resistance is elevated almost regularly. In uncomplicated arterial hypertension the pressures in the right heart and in the pulmonary circulation are within normal limits.

Cardiac work is augmented as a result of the elevated peripheral resistance or the high cardiac output. The increase in contractile force could be explained on the basis of an increase in the "afterload" of the muscle fibers, or by a transient rise in left-ventricular end-diastolic pressure associated with an efflux of potassium from the heart and/or by the presence of some inotropic factor affecting the rate of fiber shortening.[20]

PATHOGENESIS OF HYPERTENSIVE HEART DISEASE

Left Ventricular Hypertrophy

The augmented work load of the left ventricle causes an increase in its muscle mass and concentric wall thickening. Systolic blood pressure and heart weight are positively correlated.[21] Up to the "critical" heart weight of 500 gm the increase in mass is due to an increase in diameter and length of muscle cells. If the heart weight exceeds 500 gm, further enlargement takes place by an increase in the number of cells (hyperplasia) resulting from longitudinal division, together with a corresponding multiplication of the number of capillaries.[22,23]

Biochemical studies on rabbits with experimental hypertension induced by constriction of the aorta have shown that the workload on the heart causes increased net synthesis of myocardial proteins without influencing its biological turnover rate.[24,25] Furthermore, a plasma protein called cardioglobulin C has been found abnormally elevated in association with increased workload on the heart (longstanding hypertension, aortic stenosis). The cardioglobulins exert a positive inotropic effect on the isolated frog heart, possibly associated with the release of bound calcium.[26–28]

Coronary Vessels

In the hypertrophied heart the major coronary arteries are dilated and the number of anastomoses in the subendocardial plexus is increased.[29,30] The ratio of number of muscle cells to number of capillaries remains almost the same even when the heart weight exceeds 500 gm and hyperplasia occurs, because this is associated with a multiplication of capillaries.[22,23] Therefore, the capacity of the coronary vascular bed of the hypertrophied heart is increased and the coronary blood flow augmented in absolute terms but within normal range per weight unit muscle mass.[14,31] The large coronary vessels, however, do not further grow if the heart weight exceeds 500 gm, and the ratio of coronary artery capacity to heart weight deteriorates more and more.[30,32,33]

In addition, coronary arteriosclerosis develops. With regard to morphology and pathogenesis, coronary arteriosclerosis in hypertensives is similar to that observed in normotensives. Hypertension is, however, a contributory factor which promotes its development. The typical changes observed in the walls of smaller arteries and arterioles in other parts of the body, in hypertension, are not frequently or diffusely found in the vessels of the heart.

Other factors influencing the coronary blood flow through the hypertrophied heart in hypertension are: (1) the elevated arterial perfusion pressure, (2) the augmented systolic compression of the coronary vessels, and (3) the fact that the orifices of the coronary arteries in the aortic wall are not able to grow wider.

Heart Failure in Hypertension

The elevated work of the left ventricle in hypertension causes an increase in oxygen consumption. Furthermore, the basal metabolic requirements of the hypertrophied heart are augmented.[34] The adaptation processes in the coronary vessels permit a sufficient oxygen supply of the myocardium as long

as hypertrophy remains limited and significant coronary arteriosclerosis is absent. However, increasing heart weight, and deterioration of the ratio coronary vascular bed/heart muscle mass results in necrobiosis of heart muscle cells and focal fibrosis. The ensuing dilatation of the ventricle is not caused by stretching of muscle cells but mainly by dislocations of muscle fibers.[23] The disparity between coronary flow and greatly increased metabolic needs of the dilated ventricle results in myocardial decompensation.

Light microscopy and electron microscopy examinations, biochemical and biophysical studies on failing and/or hypertrophic hearts have revealed structural changes (e.g., loss of cristae, abnormalities in shape and number of sarcosomes), biochemical alterations (e.g., impairment in the cytoplasmatic NAD/NADH ratio, altered enzyme activities, deficiency in the availability or release of calcium from the endoplasmatic reticulum, reduction in cardiac norepinephrine stores), and a reduced mechanical function of sarcomeres as the result of overstretching (for references see Griggs[20]).

CLINICAL MANIFESTATIONS

Subjective Symptoms

The most frequent subjective symptom (in 42 per cent of cases, according to Bechgaard[35]) is breathlessness on exertion. This symptom, and the subsequent paroxysmal nocturnal dyspnea and pulmonary edema, are consequences of left ventricular failure. A second group of symptoms in hypertensive heart disease is related to the inadequate blood supply of the heart caused by coronary artery disease and/or increased oxygen need due to additional blood pressure elevations or physical or psychic stress. The typical complaint originating from these mechanisms is angina pectoris in its various forms.

Physical Examination

Only marked left ventricular hypertrophy with dilatation may be recognized clinically by percussion and by palpation of a laterally displaced cardiac impulse. The second aortic sound may be accentuated, but auscultation is otherwise negative. In the presence of excessive left ventricular dilatation, a systolic murmur over the mitral valve may indicate functional mitral insufficiency.

Ordinarily heart rate remains within the normal range. If tachycardia is present, cardiac failure, special types of hypertension (e.g., pheochromocytoma, acute intermittent porphyria, lead or thallium poisoning), anemia or thyrotoxicosis have to be considered. In younger patients, hyperkinetic heart syndrome might be present.

Cardiac arrhythmias and disturbances in the propagation of impulses indicate pathological changes in the myocardium caused by insufficient blood supply. The extracardiac signs of left and right heart failure are identical with those caused by heart diseases of other origin.

Radiological Examination

Concentric left ventricular hypertrophy may not be recognizable radiologically for long periods. Early signs in the standard roentgenogram are an