Cerebral Blood Flow

Physiologic and Clinical Aspects

James H. Wood

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FOREWORD

The cerebral circulation has been a subject of great interest for centuries, particularly with regard to nervous and mental diseases. The ancients ascribed many behavioral ills to the transmission of various humors to and from the brain, presumably by what is now recognized as the cerebral circulation. One can hardly resist the observation that very little, perhaps, has changed; the only difference is that now "humors" are called "neuromodulators." After the description of the circulation of the blood by Harvey in 1628, speculation about the relationship between cerebral circulation and disease became somewhat more sophisticated. Some of these speculations persist to the present day. Too much or too little blood or blood flow in the brain became suspect as possible causative factors in many disorders. For example, in 1795 Erasmus Darwin, the grandfather of Charles Darwin, reported the design of a rotating bed with which to centrifuge blood from the brain for the treatment of insomnia and mania. Cerebral ischemia, focal or otherwise, is still commonly considered to be responsible for the initiation of epileptic fits. Historically, therefore, there has been a long conceptual association between the pathophysiology of the cerebral circulation and clinical disorders, not only diseases, such as stroke, that are clearly attributable to deficient blood flow, but also many neurological and behavioral disorders.

Systematic study of the physiology and regulation of the cerebral circulation probably began about 100 years ago when Roy and Sherrington (1890) first proposed the close coupling of local cerebral metabolism to local cerebral functional activity and of local cerebral blood flow to local cerebral metabolic activity. They stated with remarkable insight and clarity that "... the chemical products of cerebral metabolism contained in the lymph which bathes the walls of the arterioles of the brain can cause variations of the calibre of the cerebral vessels ... in this reaction the brain possesses an intrinsic mechanism by which its vascular supply can be varied locally in correspondence with local variations of functional activity." The tremendous mass of knowledge about the control and regulation of the cerebral circulation that has been accumulated since the era of Roy and Sherrington has served for the most part to support their thesis.

In most of the first half of the twentieth century, studies of the cerebral circulation were largely concerned with methodology and with mechanisms for the control of cerebral blood flow. Using methods that were either qualitative or at best semiquantitative, investigators learned a great deal about the regulation of the cerebral circulation. It was established that, contrary to the view prevailing in the early part of the century, cerebral blood flow does not passively follow the arterial blood pressure but is regulated by intrinsic control of the tone of the cerebral vessels. This control is responsible for what was later enshrined with the special nomenclature of "autoregulation." It was found that chemical factors, such as carbon dioxide and oxygen tensions and pH, predominate in the regulation of cerebrovascular tone and cerebral blood flow and that neurogenic control, though present, appears to play a minor or, at least, undefined role. Much of the knowledge about the cerebral circulation that had been accumulated up to the mid-1930s was organized and presented in

Wolff's classic review (*Physiol Rev* 16: 545–596, 1936) and in the volume that represented the proceedings of the XVIIIth annual meeting of the Association for Research in Nervous and Mental Disease (Res Publ Ass Nerv Ment Dis, *The Circulation of the Brain and Spinal Cord,* Vol. 18, Williams & Wilkins, Baltimore, 1938).

The modern era in research on the cerebral circulation began with the development of methods that were not only quantitative but were also applicable to man. The nitrous oxide method of Kety and Schmidt (*J Clin Invest* 27: 476–483, 1948) was the first of this kind and was used extensively in its original form and in a variety of modifications that employed radioactive gases. Although applied in many studies of human diseases, it served to elucidate the physiology of the cerebral circulation to a degree that equalled or exceeded that of any other vascular bed. The nitrous oxide method and its modifications, however, measured the average blood flow in the brain as a whole, and many of the diseases of the brain are localized to specific regions in the brain. Based on the principles of inert gas exchange between blood and tissues that were developed by Kety (*Pharmacol Rev* 3: 1–41, 1951), methods were applicable only to the cerebral cortex, but it has become possible with emission tomographic techniques to assay blood flow in regions within the depths of the brain. With the availability of regional methods, studies of pathologic conditions became more feasible and fashionable, and, in fact, during the last twenty years or so studies of the cerebral circulation have been predominantly directed toward pathophysiology.

The present volume reflects primarily, though not exclusively, the current directions in research on the cerebral circulation. Its title reveals its emphasis. This emphasis is entirely appropriate and timely, for most of the significant new knowledge about the cerebral circulation accumulated in recent years has been in areas closely related to pathology and pathophysiology. A comprehensive and critical review of the progress made in these fields is in order and is what this book set out to perform.

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PREFACE

At a time when stroke is the third leading cause of death in the United States and clinical and surgical therapies currently used in the treatment of stroke lack the appropriate experimental proof of efficacy, the study of the physiologic and pathologic aspects of the cerebral circulation has become paramount in importance. Several recent studies evaluating clinical endpoints have been criticized for lacking the hemodynamic data required for validation of the experimental protocol. Recently, the development of experimental autoradiography and clinical positron emission tomography has allowed major advances in the study of the interrelationship between cerebral blood flow (CBF) and brain metabolism in both physiologic and pathologic conditions. The emphasis on hemodynamic aspects of brain function has been reinforced by the development of clinically employed techniques such as refinements in ^{133}Xe washout studies, the development of stable xenon computed tomographic blood flow analysis, and the validation of a single photon emission tomography. Thus, the physiologic and clinical aspects of CBF have become a major focus in neuroscience and patient care.

The purpose of this multidisciplinary reference text is to provide the sophisticated knowledge of CBF physiology and pathology necessary for the meaningful interpretation of data obtained from various types of experimental and clinical hemodynamic assessments. The methodology of reliable CBF determination and analysis is discussed with respect to individual, pharmacologic, pathologic, and possible artifactual variations. These essential factors, which ensure the validity of CBF data, are presented to aid the investigator in clinical and experimental protocol formulation and elimination of potential sources of error.

This volume was written by international experts in each field of CBF investigation and covers normal variations, congenital anomalies, atherosclerotic disease, trauma, metabolic disorders, and hemorheology with respect to historical as well as recent advances in diagnosis, evaluation, and therapy. This also examines the medical therapies for transient ischemia, acute ischemic stroke, and cerebral vasospasm, as well as prophylactic protection against ischemia. The surgical treatments of cerebral ischemia, including carotid endarterectomy, intracranial cerebral revascularization, extracranial arterial reconstruction, and recent developments in transluminal angioplasty techniques, are also objectively assessed with respect to cerebral hemodynamics.

Each chapter is extensively referenced and contains ample tables of original data, summary tables, and anatomical diagrams. Detailed illustrations of experimental and clinical techniques have been included to facilitate their practical application.

As editor, I am most indebted to the many contributing authors for their preparation of such excellent chapters and their punctual observance of submission deadlines. Dr. Louis Sokoloff, the developer of the technique of autoradiography, is thanked for his inspiring comments presented in the Foreword. Dr. Walter D. Obrist is thanked for his excellent editorial criticisms based upon his broad and thorough knowledge of CBF, and for his superb chapter contributions which help ensure the success of this project. In ad-

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I am, of course, grateful to my wife, Mary, and my parents, Naomi and Harold, for their encouragement and support.

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