CARDIOVASCULAR INNERVATION

BY

G. A. G. MITCHELL
O.B.E., T.D., M.B., CH.M., D.SC.
Professor of Anatomy and Director of the Anatomical Laboratories in the University of Manchester
Hon. Alumnus, University of Louvain

FOREWORD BY

SIR GEOFFREY JEFFERSON
C.B.E., M.S., M.CH., M.SC., LL.D., F.R.C.P., F.R.C.S., F.R.C.S.I., F.R.F.P.S., F.A.C.S., F.R.S.
Emeritus Professor of Neurological Surgery in the University of Manchester

217 ILLUSTRATIONS, MANY IN COLOUR

E. & S. LIVINGSTONE LTD.
EDINBURGH AND LONDON
1956

Made and Printed in Great Britain

CARDIOVASCULAR INNERVATION

FOREWORD

WORKS on the anatomy of the nerve supplies of the cardiovascular system are few indeed and correct accounts rarer still. Yet the subject is of great importance to medicine and one of immense fascination to the clinician. He has hitherto had to rely on texts and diagrams with rare exceptions of doubtful authenticity. Much of our knowledge of the autonomic system has been inferential, derived either from surgical experience or from physiological concepts based on experiments on animals such as the rabbit, cat and dog. It is the merit of the present work that it is about Man himself and that where recourse has had to be made to experiment, as in the pursuit of nuclear arrangements in the brain stem, the animal used has been not lower in the scale than the monkey. I think that I can say without accusation of chauvinism that Professor Mitchell won a reputation for himself as an accurate observer and, after all, accuracy in dissection and description remain what they have always been—the fundamentals of anatomy. He has now provided a basis for further advances in physiological interpretation and in surgery by furnishing a detailed account in orderly progress not only of the peripheral supply of the sympathetic and parasympathetic nerves but of their central connections. There was a time, not long ago, when it was thought sufficient for an anatomist to confine himself to descriptions and to restrain from comment or speculation as to the meaning of what he saw in a functional sense. Some regarded any over-stepping of the line as improper. But it became clear that as regards the nervous system itself its detailed anatomy was incomprehensible unless it were associated with observations on function. The reader will find that this book is in one sense a book on applied anatomy but a book with a difference—the difference being that the author is a vastly more erudite and better informed anatomist than the great majority of those who teach applied anatomy. The greatest possible care has been given to details of structure, whether gross or microscopical. The author has in fact carried out Sir James Learmonth's advice to which he refers in his preface. Those who know Professor Mitchell are aware of his deep interest in the history of medicine. It will be no surprise to them to see how brilliantly he has handled the voluminous literature of this particular subject and will acknowledge a debt to him for the immense labour which this must have cost him. It is not only a comprehensive but a well balanced account. History is a plastic sort of material that can be safely handled only by men of good judgment.

Mention was made of the stress laid on the functional significance of the plan of the autonomic system (a system no more " autonomous " than any individual living linked to a close society). This is well illustrated by the chapters on its central representation in the brain as a whole, one so important in psychosomatic medicine and indeed important to any clinician. Of equal interest will

be the chapter on afferents in the sympathetic nervous system, where the author feels that his evidence is strong enough for him to make a break with traditional teaching.

I personally welcome this book and am happy to express my gratitude to Professor Mitchell for having carried so difficult a task to so admirable a conclusion.

GEOFFREY JEFFERSON.

Manchester, December, 1955.

PREFACE

ALTHOUGH a great deal is known about the innervation of the heart and vessels and about the possible central connections of this vital neurovascular complex, the subject receives scant attention in all the well-known anatomical treatises. Apart from *Le Systême Neurovasculaire* (1949) by G. Lazorthes, which deals excellently with several aspects of the matter, one knows of no publication which is devoted exclusively to it or which provides a reasonably complete and systematic account of present knowledge. Indeed, the best anatomical descriptions available in English are to be found in the latest editions of books such as those of White, Smithwick and Simeone (1952) and Kuntz (1953), but as they are devoted mainly to the clinical and functional aspects of the autonomic nervous system the anatomical accounts are relatively brief.

My own interest in the subject of autonomic innervation was stimulated in 1933 by Sir James R. Learmonth, and for many years I have been attempting, often with the valued aid of colleagues who have studied particular problems, to verify and extend existing knowledge in this branch of neurology. Having accumulated a large number of observations, particularly on the cardiovascular system, I approached Sir J. R. Learmonth with the suggestion that I might record them in book form. He advised me to write first an up-to-date and balanced account of the central and peripheral parts of the autonomic nervous system, and this led to the publication in 1953 of my *Anatomy of the Autonomic Nervous System*. Thereafter I turned again to the idea of producing a monograph on the subject of cardiovascular innervation because of its especial theoretical and practical importance. To this end I selected relevant details from the extensive literature, confirming and augmenting them wherever possible by the results of my own investigations, reviewing and occasionally modifying existing hypotheses, and blending all these disconnected observations and opinions into a composite picture.

The result of these efforts forms the basis of this work, which is primarily anatomical and concerned with Man. The study of structure cannot be divorced from morphological, embryological, physiological, pathological and clinical considerations, and information from such sources is utilized freely if it helps to explain or illumine certain points. The provision of complete details in these other fields, however, is not the chief aim, and those desiring further information about specific problems should consult the books or articles referred to in the various chapters. The neurovascular complex is so vital in the animal economy that it influences the state and well-being of every part of the body, and often it is so closely integrated structurally and functionally with other forms of innervation that it cannot be dissociated from them. This has necessitated the inclusion of a certain amount of information about visceral nerve supplies, but this has been reduced to the lowest limits possible. Complete understanding still evades us as many points yet remain to be discovered, but by the combined efforts of many workers the clouds at present obscuring our vision will ultimately be swept away.

G. A. G. MITCHELL.

Manchester, December, 1955.

ACKNOWLEDGMENTS

MY cordial thanks are due to Sir James R. Learmonth, my first and esteemed mentor in autonomic neurology, and to Sir Geoffrey Jefferson who inspires everyone, and most of all those who have the privilege of being his colleagues: I deem it a signal honour that he wrote the Foreword to this book. My earlier investigations were carried out at Aberdeen University with valued support from the Medical Research Council, and since the war they have been continued with the aid of the excellent facilities provided by the Authorities at Manchester University, guided by the kindly and informed interest of Sir J. S. B. Stopford, and assisted by liberal financial support from the Nuffield Foundation and Professor John Morley. My thanks are also due to Sir Harry Platt, Professor E. D. Telford and Professor Crighton Bramwell for their interest and encouragement, and to Professor J. C. White of Boston and Professor H. A. Meyling of Utrecht for many favours.

I owe much to Miss D. Davison for her resource, care and artistry in composing beautiful drawings from my imperfect dissections and sketches; and I am grateful to all those who readily allowed me to reproduce illustrations or photomicrographs and whose help is acknowledged in individual legends.

Many members and ex-members of my staff and Honours B.Sc. students in Anatomy—Doctors E. R. A. Cooper, E. L. Patterson, F. R. Wilde, R. Warwick, G. T. Ashley, E. P. Samuel, B. H. Dawson, K. Rushton, and M. J. Waas, Miss E. M. Ainscow, Miss S. A. Naylor, and D. Mayor, R. Brown, F. B. A. Cookson, A. J. Chadwick, A. W. F. Fisher, M. Segal and J. S. Whittaker—have assisted me in investigating various problems or in interpreting histological, experimental and embryological findings, and have generously allowed me, when required, to quote their findings or use their preparations.

I am indebted to members of staff of the Aberdeen and Manchester University Libraries, and especially Mr. G. Wilson and Mrs. E. M. Parkinson, for tracing and obtaining numerous books and journals; to Mrs. J. E. Kern for secretarial help; and to Messrs. H. Gooding, C. K. Pearson, P. Howarth, J. Graham, W. Carnie, A. Cain and the late Mr. J. Moir, who at various times and in different places have placed their technical skills at my disposal. To my wife I owe a particular debt of gratitude for sharing patiently the burdens of translation, revision and proof corrections.

Lastly, it is a pleasure to record that the complicated process of book production seems deceptively easy when one is steered past every difficulty by such experienced pilots as Mr. C. Macmillan and Mr. J. Parker of Messrs. E. & S. Livingstone.

CONTENTS

CHAPTER I

GENERAL INFORMATION

THE heart and vessels are innervated by the autonomic component of the nervous system which governs all visceral and vascular activities and a knowledge of the arrangement of this system is therefore essential for an understanding of such matters as vasomotor control by higher nervous centres and the origins, nature, connections and pathways of fibres concerned with vascular innervation. Our information about the autonomic nervous system is still imperfect and much of it is derived from experimental anatomical and physiological studies on animals far removed from *Homo sapiens* in the complexity of their nervous organization. This must be borne in mind when evaluating the evidence presented.

THE AUTONOMIC NERVOUS SYSTEM

The subdivision of the nervous system into somatic and autonomic components is rather artificial, although it is convenient for descriptive purposes. Anatomically they are neither separate not distinct entities. They originate from common primordial cells, they develop together, they are built up from the same basic units or neurons associated in similar reflex arcs, they comprise central and peripheral parts, and structurally they are always related and often closely connected. The title autonomic should not be interpreted too literally as indicating that this part of the nervous system is self-governing or independent, or that there is no interaction between the somatic and autonomic components. In an intact animal it is probable that all so-called autonomic activities are in fact under the control of the nervous system, either directly, or indirectly through its influence on the endocrine glands. Owing to their close morphological relationships somatic and autonomic reactions are seldom entirely distinct, and many somatic activities—*e.g.*, violent exercise, to mention only one—would be impossible without the associated complex readjustments in the cardiovascular, respiratory and other systems.

Definition

The autonomic nervous system has been variously referred to as ganglionic, organic, vegetative, visceral, splanchnic and involuntary, and it may be defined as the part regulating all these bodily processes which are not under voluntary or volitional control, with the probable exception of postural activities. Thus it is concerned with the regulation of circulatory, respiratory, alimentary,

excretory and reproductive functions, being closely associated in some of these activities with certain ductless glands such as the hypophysis cerebri and suprarenals. To effect this control it receives stimuli from the heart, vessels, lungs, alimentary tract, kidneys and other viscera and transmits appropriate impulses to the same structures. It is closely implicated in emotional reactions and influences behaviour and personality, but the respective parts played by the autonomic and somatic components of the nervous system in these phenomena are not yet established.

Many writers have defined it as a purely efferent system, a limited view taking no cognizance of the fact, clearly recognized by Hughlings Jackson (1873) and others, that visceral and vascular functions are represented at all levels in the central nervous system and proper central control is impossible without afferents. Gaskell and Langley are often quoted as the authorities for the belief that the autonomic nervous system is purely efferent, but Gaskell (1886) refers specifically to splanchnic afferents in the visceral nerves and the probability that they are connected with cells in the posterior grey columns of the spinal cord, adding " we must look upon this sensory cell column as double, one part belonging to the somatic and the other to the splanchnic sensory nerves, in precisely the same way as the motor cell column has been separated into an anterior somatic and a lateral splanchnic cell column." It is true that Langley's writings do seem to indicate that he regarded the autonomic nervous system as an efferent mechanism, but he did state briefly (Langley, 1903, 1921) that afferent fibres do exist in sympathetic and parasympathetic pathways, although he regarded them as belonging to the somatic system. Others have also adopted this view. Thus Kuntz (1953), while admitting visceral afferents exist, excludes them from the autonomic nervous system because they enter the neuraxis through cerebrospinal nerves, but this is irrational, for all preganglionic fibres in the autonomic outflow also pass through cerebrospinal nerves and nerve roots.

Extent

The autonomic system, like the somatic, consists of central and peripheral parts. The *central* elements are intrinsic parts of the central nervous system, being located in the cerebral cortex, thalamus, hypothalamus, cerebellum, brain stem and cord, and being interconnected by various tracts. The *peripheral* parts consist of two paravertebral ganglionated trunks which extend along the entire length of the anterolateral surfaces of the spinal column; various prevertebral and visceral nerve plexuses and their branches in the neck, thorax and abdomen; besides autonomic fibres which are inherent constituents of most cerebrospinal nerves. Both central and peripheral parts are described more fully in subsequent chapters.

The Basic Arrangement

The regulation of autonomic functions is essentially automatic, although influenced by *higher* " *centres* " in the central nervous system. The regulation

of visceral and vascular functions depends ultimately on the control exercised by these " centres," although it is typically " involuntary " in contradistinction to the control of somatic activities which is mainly " voluntary." It is known, however, that certain functions usually regarded as involuntary can be influenced voluntarily or volitionally. Thus reports have been published of individuals who could control at will pupillary (Bechterew, 1895) and pilomotor activities (Maxwell, 1902; Chalmers, 1904), or who could produce local (Mitchell, 1884) or generalized (Kennard, 1937) vasomotor changes, while Favill and White (1917) found records of thirteen persons with some voluntary control over the rate of their heart beats; of course the abnormalities produced by disease or injury often lead to alterations in the regular pattern of autonomic reactions, and of these

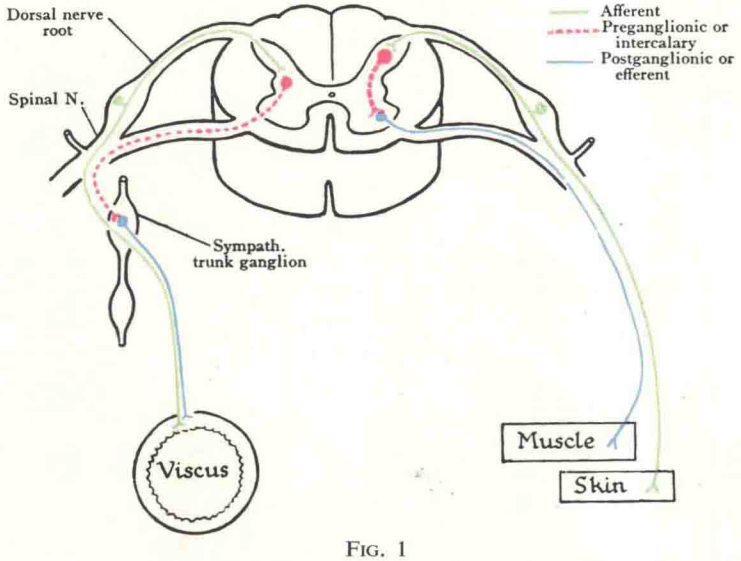

FIG. 1
Diagram of autonomic and somatic reflex arcs revealing their fundamental similarity.

vasomotor changes are amongst the most common. Reflex autonomic activity of a kind can occur through anatomical pathways independent of the brain and spinal cord, but the complex co-ordination required, for example, for homeostasis, necessitates an overriding control by higher autonomic and somatic nervous centres operating in integrated harmony.

Both autonomic and somatic components are constructed from the same basic units—afferent, intercalary and efferent neurons—linked together as reflex arcs (Fig. 1). In the autonomic component the outgoing pathway is interrupted by a synapse in a peripheral ganglion, so that *preganglionic* and *postganglionic** elements are described, whereas the somatic outflow is

* The term postganglionic is now often used to denote not only the truly postganglionic fibres but also their parent cells. Strictly speaking these cells are ganglionic as they are located in the actual ganglia, whereas their axons are postganglionic in the sense that they are after or beyond the ganglia. It has been suggested that ultra-ganglionic would be a better description, but the distinction is finical, and there is no necessity to replace a well-established term which is unlikely to mislead anyone.

uninterrupted. There is no fundamental difference, however, in the arrangement, but merely a difference in the location of the efferent cells. Initially the autonomic and somatic components develop in close relationship in the basal lamina of the developing neural tube (Figs. 2, 3), but later in embryonic life groups

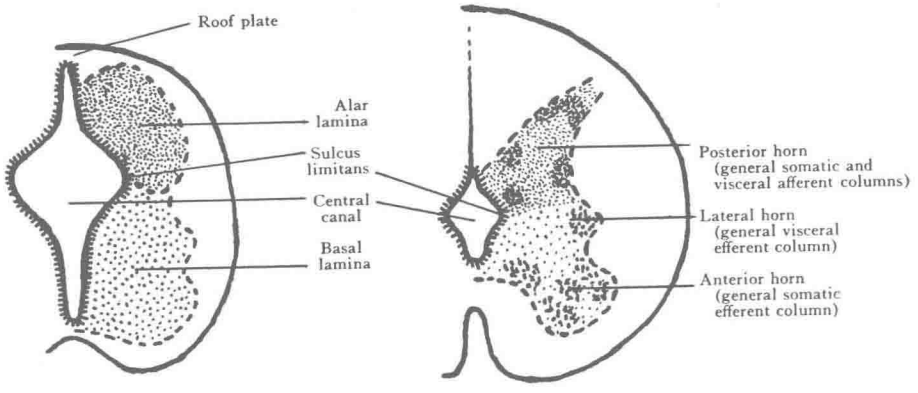

FIG. 2

Differentiation of cell columns in developing medulla spinalis.

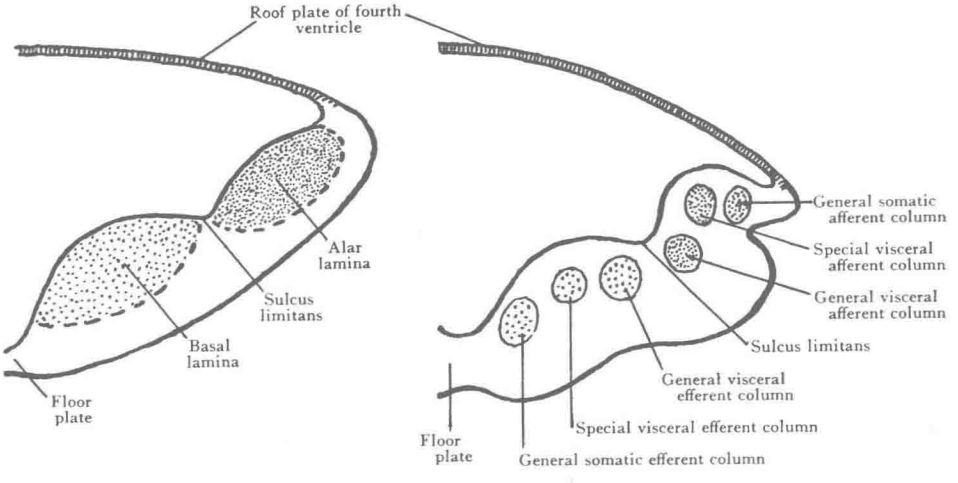

FIG. 3

Differentiation of cell columns in developing medulla oblongata.

of cells migrate outwards from the neural tube to form peripheral ganglionic masses (Figs. 4, 5, 6) such as the ganglia associated with the cranial nerves and those of the sympathetic ganglionated trunks. These are the efferent autonomic cells and to maintain anatomical and functional relationships the intercalary (connector or preganglionic) axons must follow these cells and so wander outside the central nervous system to form synapses in peripheral ganglia. This fact must be appreciated, since it is customary to describe the autonomic efferent pathway as