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An introduction to basic and clinical concepts

second revised and enlarged edition

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Foreword to the second revised edition

A great part of man's nervous system is concerned with activities of which he is essentially unconscious and over which he has little or no voluntary control. Claude Bernard opined that perhaps a divine providence considered them too important to entrust to a capricious will. "We are thrust into this world by smooth muscle, which is under the control of the autonomic nervous system. From moment to moment we are dependent for our conscious existence on the moderate contraction of the blood vessels, routinely kept in this state by autonomic impulses. Most of the complicated processes of digestion, from the initial outpouring of saliva to the final riddance of waste, require the participation of autonomic nerves. Any vigorous exercise in which we may engage depends upon cooperation of autonomic government of appropriate effectors; thus throughout eons of past time the physical struggle for existence has been made possible by that government . . . which preserves the stable states of the fluid matrix that are required for ready response to every call to action."

Once the brilliant studies of Gaskell and Langley had brought to light the importance of the involuntary or vegetative nervous system to the efficient functioning of the human organism, physiologists the world over, led by Walter B. Cannon whose ideas are quoted above, set themselves to elucidate the principles of its action in such fundamental activities as the maintenance of 'le milieu interne' necessary for health, the continuation of the race and the natural reflex mechanisms of controlling glands and smooth muscles. But until comparatively recent times, relatively neglected was the manner in which the autonomic nervous system participates in medical and neurological diseases, or itself may be selectively deranged by pathologic processes.

In the past decade or two, clinical investigators have begun to rectify this deficiency. A number of singular advances in the neurology of the autonomic nervous system

have been made. A form of pure autonomic polyneuropathy has been identified and in several other types of polyneuropathy the autonomic and pain fiber bear the brunt of the disease. A series of central nervous system diseases have been discovered in which spinal and hypothalamic centers degenerate. And for the first time the pathology of the sympathetic nervous system has been surveyed in most of the important medical and neurological diseases. Neuropathologic experiments have been done on the autonomic nervous system in animals in the hope of clarifying human diseases.

Professor Appenzeller has presented the medical profession with a valuable monograph devoted to these and other pertinent topics. The warm reception given the first edition and the surge of new information that he has garnered from the recent literature have encouraged him to update the subject and favor us with a second edition. His efforts should reward the interested reader whether of neurological or general medical bent.

Raymond D. Adams, M.D.
Bullard Professor of Neuropathology,
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Boston, Mass., U.S.A.

Foreword (first edition)

It seems paradoxical that progress in understanding of diseases of different parts of man's nervous system is almost in inverse proportion to the complexity of the structures involved. More explicitly, we appear to be much more familiar with diseases of the complex cerebral and cerebellar cortices or the basal ganglia than we do about those of the peripheral nervous system, which is infinitely simpler and more uniform in structure. And, of the many diseases of the peripheral nervous system those of the autonomic parts are certainly the most obscure. It is not that medical scientists have neglected the autonomic nervous system, for its anatomy and physiology are the subjects of a voluminous literature, but rather that its clinical disorders and their pathology have not been studied systematically by appropriate histological techniques. The few articles that have appeared have consisted of little more than blind surveys of random samples of sympathetic ganglia and nerves and, as expected, were notably uninformative.

Professor Appenzeller reminds us that in recent years this unfortunate state of affairs is being repaired to some extent. Gradually and almost unobtrusively new diseases that exert their predominant effects on the sympathetic and parasympathetic nervous system have been discovered. When he places them alongside one another, they obviously have come to represent a fairly respectable body of clinical medicine and neuropathology findings. Moreover, it appears that scattered studies of the autonomic nervous system, in some of the standard diseases of man's brain and spinal cord, are beginning to yield unexpected results. In Parkinson's disease, for example, den Hartog Jager has found Lewy type of inclusion bodies in the sympathetic ganglion cells in a large proportion of cases, which may explain their well-known tendency to orthostatic hypotension and fainting; and other examples are to be found.

The chief merit of this work is that it brings together in the confines of one small monograph the salient facts about this new group of autonomic nervous diseases. But it does more for the neurologically oriented reader. Being himself knowledgeable about the physiological techniques whereby this part of the nervous system can be evaluated in living man the author is able to review in a useful fashion some of the current clinical neurophysiological methods for the study of this part of the nervous system. And, finally in the interest of presenting a well-rounded view of his subject, he concludes with an extensive discussion of the role of the central integrative centers of the autonomic nervous system in some of the more complex biological activities of man.

This small monograph should prove to be a welcome addition to a growing number of systematic studies of the peripheral nervous system.

Raymond D. Adams, M.D.

Introduction to the second revised edition

The rather modest size of the first edition published in 1970 has grown to the present volume. This increase in size requires some explanation. Over the past few years, clinical and pharmacologic research has led to new insights into the pathogenesis and therapeutic possibilities of disorders affecting the autonomic nervous system. A particularly noticeable advance was made in the understanding of neurochemical processes and clinical manifestations associated with deficiencies of some central and peripheral neurotransmitter mechanisms. Impetus to the publication of the second edition was given by the widespread appreciation of autonomic dysfunction in disorders of many systems and the need to attend to autonomic clinical deficits in the management of patients with a variety of diseases.

In the past, the assessment of autonomic deficits was largely based on anecdotal accounts and patients with predominant autonomic dysfunction were often reported as medical exotica. This early stage of the advancement of knowledge is now fortunately past and objective tests of autonomic function can now be applied to help pinpoint the site of lesions. Therapeutic possibilities have become a reality and the wide dissemination of knowledge to the lay public about autonomic dysfunction has made it necessary for practicing physicians to become thoroughly acquainted with this part of nervous activity in health and disease. These considerations and the wide scatter of recent advances in this area in disparate publications has led to the collection of up-to-date relevant information in the second edition.

Though the plan of the first edition has been preserved, new chapters have been added including some on biofeedback, monoamines and autonomic dysfunction in hypertension. Because of widespread autonomic dysfunction in patients with spinal lesions, a chapter is devoted to the clinical significance of these disorders. Once again,

I am most grateful to ASP Biological and Medical Press for their expert help and unflagging support in bringing this project to fruition.

Otto Appenzeller
Albuquerque, New Mexico
February, 1976

Introduction (first edition)

This book does not intend to give a complete survey of the autonomic nervous system, rather it is the aim to present to the student and practicing physician, useful information which might help in the understanding of autonomic function and the application of this information to relevant clinical settings.

In the last decade, tremendous advances have been made with the use of sophisticated methods of investigation. Clinicians, however, have developed a fairly rigid view of autonomic function, apparently uninfluenced by experimental results. It is the purpose of this book to select experimental findings of clinical significance and put them into perspective by comparing them with clinical data on autonomic dysfunction.

Anatomically, the term 'system', as distinct from an organ, is used to designate tissue which might be in different topographic areas of the body, but which is functionally related. In the autonomic nervous system, two functional subdivisions can be recognized. The ergotropic system which is concerned with preparedness of the body and so-called 'animal functions', and the trophotropic system which is mainly responsible for the fluctuating activity of organs. The ergotropic system corresponds peripherally with the sympathetic nervous system, whereas the trophotropic system is predominantly parasympathetic. In the central nervous system this anatomical distinction becomes blurred, but the structures concerned with sleep may be part of the trophotropic system.

The autonomic nervous system is concerned with the regulation of three main functions; the somatic or animal function, by which responses to changes in environment are made predominantly by appropriate active measures; the regulation of organ function, which is concerned with rest and activity of organs; and endocrine function, which influences the entire organism. The endocrine system is closely integrated with

nervous activity through the hypothalamus and pituitary centrally, and also peripherally through the release of neurohumors in response to appropriate stimuli. This system is dealt with extensively in neuroendocrine texts, and will only briefly be considered in this book.

While in the past physiological experimentation was closely tied to morphology, more recently pharmacology and neurochemistry have been used to investigate the function of the autonomic nervous system. Nowadays electronmicroscopy and histochemistry once again allow a close association between morphology and physiology advancing knowledge at the cellular level. For this reason, in this book anatomical and physiological considerations precede clinical discussions.

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Some illustrations have been obtained from other sources. In all cases reference is made to the original publication in the legend. The full source is recorded in the reference list at the end of the book. Permission for reproducing this material is gratefully acknowledged.

Acknowledgements (first edition)

This book would not have been written without the understanding support of my wife, to whom it is dedicated. I am also grateful to her for reading the manuscript. My thanks are due to Mrs. Grace Wilson, Mrs. Polly Gauthier and Mrs. Vi Farmer for typing the manuscript. Many students and residents in neurology have contributed by helpful discussions, but my indebtedness is particularly great to Drs. T.K. von Storch and G.B. Marcus, and to Mr. D. Scott. Finally, the editors and publishers of the Handbook of Clinical Neurology have generously allowed the use of material previously published.

Contents

CHAPTER 1

Anatomy and histology

Galen (1528) seems to have been the first to refer to a part of the autonomic nervous system when he described a nerve trunk lying along rib heads and recognized its connecting fibers with the spinal cord. He thought that this was a branch of the vagus and believed that through it the viscera received sensitivity from the brain and power to move from the spinal cord. Galen also observed at least three enlargements along the course of the sympathetic chain and described the ganglion at the entrance of the chain into the abdomen, which might have been the semilunar ganglion of the celiac plexus. He suggested, a widely accepted belief thereafter, that there was 'sympathy' or 'consent' between body parts and regarded the peripheral nerves as tubes through which animal spirits were distributed to bring about this 'sympathy'.

Galen's belief that the vagi and sympathetic trunks were a single unit, both functionally and anatomically, was shared by subsequent anatomists until Estienne (1545) recognized the sympathetic trunk as a distinct anatomical structure. Willis (1664) gave the name of 'intercostal nerve' to the sympathetic trunk and believed that the cerebellum was responsible for involuntary movements which he distinguished from voluntary motion.

Although Willis recognized the innervation of the heart by the vagus nerve, the functional significance of this was not discovered until Lower's (1669) description of the effects of vagus section on heart rate.

The suggestion that involuntary movements are initiated by local stimulation due to nerve irritation is attributed to Whytt (1751) and he used this as an explanation for the reaction of the pupil to light. Whytt's importance to neurophysiology is further enhanced by his suggestion tnat all 'sympathy' or 'consent' must be referred to the central nervous system since it occurs between body parts whose nerves make no connection with each other so that the transmission of 'sympathy' cannot involve the flux of matter and must therefore occur in an area where all nerves have their origin (Whytt, 1765).

Du Petit (1727) pointed out that the sympathetic trunk was not directly connected with

the brain and was a separate structure from the vagus, but it was Winslow (1732) who first designated the paravertebral chain as 'the great sympathetic nerve'.

In 1764 Johnstone suggested that the movements of the heart and intestine are involuntary because the sympathetic ganglia blocked the actions of the will and prevented them from reaching these structures and that this blockade also accounted for the relative insensitivity of the viscera.

Studies by Bichat in 1802 led to the concept of 'animal life' and 'organic life'. He pointed to the continuous action which was the hallmark of organic life distinct from the intermittent activity of animal life, a concept which is still widely expressed by the terms 'visceral' and 'somatic' respectively. Bichat was aware of the different appearances of gray and white rami communicantes but did not recognize their significance.

The term 'vegetative nervous system' was used by Reil (1857). He thought that the rami communicantes served as connectors between the animal and vegetative nervous systems. An early description of nerve cell bodies in sympathetic ganglia appeared in Ehrenberg's (1833) writing, together with comments on the microscope structure of nerve fibers. In the 19th century the ciliary, sphenopalatine, otic and submandibular ganglia were thought of as part of the autonomic nervous system but their functional significance was not appreciated.

Meissner's (1857) mention of the submucous plexus and the description of the myenteric plexus by Auerbach (1864) in the second half of the 19th century concluded the anatomic studies which paved the way for the physiologic work on vasomotor function by Bernard (1878). His studies led to the concept of sympathetic vasoconstrictor action but not until some time later was he able to demonstrate vasodilator nerves in arteries supplying the submandibular gland after stimulation of the chorda tympani. Bernard thought that the sympathetic reflexes were mediated by the spinal cord and that on stimulation of some areas of the brain impulses were discharged through the sympathetic fibers.

Gaskell (1886) gave a detailed description of the anatomy of the rami communicantes and recognized that the efferent fibers within these nerves arise in the spinal cord and that corresponding fibers can be found in some cranial nerves. He also recognized the connection with the central nervous system of the peripherally located ganglion masses through medullated fibers and divided these fibers into bulbar, thoracolumbar and sacral groups. Langley and Dickinson (1889) used the action of nicotine on ganglia to study the relation of the nerve fibers to the peripheral ganglion cells and proposed the name 'autonomic nervous system'. When this term was coined the different distribution and functional effects of the thoracolumbar and craniosacral outflows were known and Langley separated the former from the rest of the autonomic nervous system. After the discovery of substances which either produced actions similar to those obtained by stimulation of the thoracolumbar or of the craniosacral outflows he coined the term 'parasympathetic' for the latter (Langley, 1901).

Anatomy of the autonomic nervous system

Body functions, which can proceed independently of volitional activity, are regulated at least in part by reflex mechanisms served by afferents, efferents and central integrating structures which are included in the autonomic or vegetative nervous system. Although the activity of this system is essentially autonomous, it is not