The involuntary nervous system / by Walter Holbrook Gaskell.

Monographs on Physiology

THE INVOLUNTARY NERVOUS SYSTEM

W. H. GASKELL

THOMAS LEWIS.

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EDITED BY

ERNEST H. STARLING, M.D., D.Sc., F.R.S., F.R.C.P.

THE INVOLUNTARY NERVOUS SYSTEM

BY

WALTER HOLBROOK GASKELL

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AUTHOR OF "THE ORIGIN OF VERTEBRATES," ETC.

WITH COLOURED FIGURES

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EDITOR'S PREFACE

In no science is the advance at any one time general. Some sections of the line are pushed forward while other parts may remain for years with little movement, until in their turn they are enabled to progress in consequence of the support afforded by the advance of the adjacent sections. The increasing number of series of monographs in different sciences is a recognition of this fact, as well as of the concentration of interest which characterizes this age of specialization.

In the present series it is intended to set out the progress of physiology in those chapters in which the forward movement is the most pronounced. Each monograph will contain an account of our knowledge of some particular branch of physiology, written by one who has himself contributed in greater or less degree to the attainment of our present position. It is hoped that by securing the help of men who are actively engaged in the advance of the subject the outlook of each monograph will be forwards rather than backwards. An exhaustive account of previous writings on the subject concerned is not aimed at, but rather an appreciation of what is worth retaining in past work, so far as this is suggestive of the paths along which future research may be fruitful of results. The more valuable the monographs in inspiring the work of others, the greater will be the success of the series.

The death of Dr. W. H. Gaskell, just after he had completed the MS. of the present volume, deprived us of a

leader in physiology whose work and ideas for many years dominated the labours of English physiologists. It is to him above all others that we owe our present knowledge of what he terms "the involuntary nervous system," and it was fitting that an account by him of his life's work should form the initial volume of this series of English monographs.

In all his work Gaskell was never content with the mere record of a new fact. The ever-recurring question was "What does this mean?" and the search after the meaning of phenomena led him to wide generalizations, parts of which indeed may not stand with future investigation, but all of which have served and will serve as a beacon light in revealing problems and showing the way of research to those working in allied branches of the subject.

ERNEST H. STARLING.

October, 1915.

PREFACE

I WENT to Leipsic in 1874 to Ludwig's Laboratory with the intention of working at problems connected with the sympathetic nervous system, and from that time until now my thoughts have been occupied with the meaning of this nervous system and with problems which have arisen from its study, such as the origin of the vertebrate central nervous system and thence the origin of the vertebrates themselves.

On my return to England, at the request of Professor Foster, I gave some lectures on the innervation of the vascular system, which led to a course of lectures on the sympathetic and allied systems of nerves. These lectures have been continued from year to year up to the present time, and at the request of some of my past students I have determined to publish an epitome of them in book form, in order to put before the world the part which my researches have played in the elucidation of the problems concerned with the innervation of involuntary muscular systems. I am especially inclined to do this now, because recent researches have thrown so much light on the origin of the cells of the sympathetic nervous system and their close relations with the chromaffine cells, that I am able to present to my readers a consistent and harmonious account of the plan of innervation of all the involuntary muscular systems in the higher vertebrates both from a physiological and from a morphological point of view. I have been guided throughout all the investigations I have ever made by the feeling that the broader physiological

problems cannot be satisfactorily solved without the assistance of morphology, and conversely that the larger morphological problems, such as those concerned with evolution, must take into account the facts of physiology. It is this guiding principle which is responsible on the one hand for the "Origin of Vertebrates" and on the other for the present treatise.

W. H. GASKELL.

DURING the two months before my father's death, I was engaged with him in revising the various chapters of the present work.

This revision was completed a few days before his death; only one or two paragraphs here and there not having been satisfactorily written. He then told me that on the whole he was satisfied with the form of the book, and that it represented fairly accurately his views on problems to which he had devoted his life.

He had not, however, fully collected and arranged the many references: I have thought it better to leave unaltered certain quotations and references from books, later editions of which had been published than the one quoted. There are also certain passages about which he talked to me, with which he was not entirely satisfied, but I have thought it better to leave them as written, rather than to attempt to modify them. The diagrams had also been approved by him, though no actual descriptions of them had been written out; for these descriptions I am responsible. I desire to express my thanks to Mrs. Thacker for help with the author's index and references, and to Miss Alcock for the subject index.

J. F. GASKELL.

THE UPLANDS,
GREAT SHELFORD *September*, 1915.

CONTENTS

CHAPTER I

THE HISTORY OF THE INVOLUNTARY NERVOUS SYSTEM

THE muscular tissue of the body is divisible into two well-marked groups, the voluntary muscles and the involuntary muscles; terms which in themselves imply a distinction between the nervous arrangements connected with these two groups of muscles. We may therefore look upon the nervous system as composed of two parts, the one connected with the movements of voluntary muscles, and the other with those of involuntary muscles. The former part may be termed shortly the voluntary nervous system; and the latter, the involuntary nervous system.

Our knowledge of the methods, by which sensory stimuli are converted into action, is chiefly based upon investigations of the voluntary nervous system; and has led to the conception that the nervous system is built up of a series of neurons, through which all the complicated movements can be effected. In the vertebrate a reflex action in the spinal cord is caused by a sensory stimulus, which travels from the periphery along a sensory nerve to a nerve cell in the ganglion on a posterior root, and thence by a root fibre to make communication with some cell or cells in the central nervous system itself. This primary or sensory neuron has been called the receptor element, and its parts consist of a sensory nerve cell, a sensory nerve fibre and a sensory root fibre; the last is not confined to its own segment in the cord, but communicates with other segments, some near, some far away. In all cases these root fibres ultimately make connexion with another neuron. In the simplest case this other neuron may consist of a motor cell with dendrites and with an axon which goes direct to the muscles and forms its motor nerve fibre. This neuron has been called the excitor element. However, in most cases, possibly in all, the receptor element does not connect directly with the excitor element, but an intermediate neuron in

the central nervous system unites the two; this I shall call throughout this book the "connector element."

When these three neurons belong to the same segment, the reflex may be termed a primary or segmental reflex; and the connector neurons concerned in such reflexes may be called primary connector neurons (Fig. 2, A).

A connector neuron does not necessarily communicate directly with an excitor neuron but may only connect after a series of communications with other connector neurons, which thus form a series of relays between the receptor and excitor elements. By means of this relay system of connector neurons the higher centres of the nervous system are brought into harmony with the segmental mechanism. The connector neurons of these relay systems may be called secondary connector neurons.

The axon of a connector neuron cannot be called a motor or a sensory nerve fibre; I propose therefore to call it simply a connector fibre. When such connector fibres are grouped together in definite parts of the central nervous system, they are called tracts, which are designated as ascending or descending according to the position of the nerve cells, of which they are the axons. The great characteristic of these connector nerve fibres is the formation of collaterals, by means of which each nerve fibre connects with more than one neuron.

In all cases the receptor neurons of the voluntary system are found in the posterior root ganglia both in the cranial and spinal regions, and the excitor neurons in the groups of nerve cells found in the central nervous system, which form the motor centres and give origin to the motor nerves of the voluntary muscles. These motor cell groups are not situated in the same position in all parts of the central nervous system. We have every reason to believe that the central nervous system of the vertebrate indicates a derivation from a segmentally arranged nervous system, such as is found in the higher forms of invertebrates, and the nerves which supply these segments form a succession of segmental nerves, which commence just posterior to the infundibulum and form a great group of nerves extending to the end of the body. They may therefore be termed infra-infundibular, in contradistinction to the nerves of special sense, olfactory and optic, which arise from the supra-infundibular region of the central nervous system. These infra-infundibular segmental nerves,

which correspond to the infra-œsophageal nerves in the invertebrate, are divisible into cranial and spinal segmental nerves, supplying motor fibres to the voluntary muscles of the cranial and spinal segments respectively.

I pointed out in 1889 that the spinal and cranial segmental nerves differed in that the former arose from the central nervous system by two roots, ventral and dorsal, but the latter from three roots, ventral, lateral, and dorsal, and that the cranial region must be looked upon as more primitive than the spinal; so that the three-root system was more likely to give a clue to the segmental arrangement in the invertebrate ancestor than the two-root system. The work of V. Wijhe has given an explanation of the lateral root; for he has shown how in the embryo of the selachian the mesoblast in this cranial region has a double segmentation, and forms a dorsal and ventral series of segments out of which the muscles are developed. The muscles developed from the dorsal series are the eye muscles, and those supplied by the hypoglossal nerve. Those developed from the ventral series are the muscles supplied by the motor part of the trigeminal, the facial, the glossopharyngeal and the vagus, that is to say the muscles concerned with mastication and respiration. This double segmentation has been called respectively mesomeric and branchiomeric; but because the latter includes the segments concerned with mastication, which have nothing to do with respiration, I called the ventral segmentation the splanchnic or visceral segmentation in contradistinction to the dorsal, which I called the somatic segmentation.

In my book on the "Origin of Vertebrates" I have put forward my conceptions of the manner in which the voluntary muscles of vertebrates arose from the corresponding muscles of invertebrates.

In the invertebrate (Limulus, Scorpion, etc.) the animal is divided into segments, which may be considered as forming a double segmentation, that of the body and that of the appendages, so that the voluntary musculature in these animals falls naturally into two groups, (1) the body musculature, (2) the appendage musculature. The body or somatic musculature forms in all cases the great longitudinal muscles and the dorso-ventral muscles. In the vertebrate the longitudinal muscles are found in the trunk region and are divided segmentally to form the

myotomes; the dorso-ventral muscles are found in the cranial segments and form the ocular muscles. This segmentation I have therefore called in both vertebrates and invertebrates the somatic segmentation.

The striated muscles in the vertebrate, which are derived from the invertebrate appendage muscles, are situated mainly in the cranial region, and form two groups in the adult vertebrate; (1) the muscles of mastication, which correspond to the muscles of the masticatory appendages in the invertebrate, and (2) the muscles of respiration, which correspond to the muscles of the respiratory appendages. Therefore the segmentation due to the appendages in the invertebrate corresponds to V. Wijhe's ventral segmentation, which I have called splanchnic or visceral. In using the terms somatic and splanchnic to denote these two segmentations instead of the terms mesomeric and branchiomeric, I was dealing throughout only with striated musculature, so that the term somatic denoted a well-defined group of striated body muscles in contradistinction to another well-defined group of striated visceral or splanchnic muscles. It is therefore absolutely erroneous to make use of the term somatic as defined by me, as though it were synonymous with striated, as has been done by Edinger and by Langley and Anderson.

In Limulus and the Scorpions the region which bears the masticating appendages has been called the prosomatic region, and the region which bears the respiratory appendages the mesosomatic region. The same terms may be used with advantage in talking of the corresponding regions of the vertebrate.

The more primitive arrangement of the segmental motor nerves in the cranial region to supply the muscles belonging to the somatic and splanchnic segments, corresponding to the somatic and appendage muscles of the invertebrate, is naturally shown also in the origin of the motor fibres from the motor-cell groups in the cranial region. Thus in the prosomatic region (Fig. 1) the nucleus masticatorius of the trigeminal together with the series of nuclei, which are described on the so-called descending root of the trigeminal and give origin to the fibres of this so-called root, represent the motor neurons of the splanchnic segmentation, and represent therefore the motor neurons of the muscles of the prosomatic appendages; they are quite separate from the oculomotor and trochlearis nuclei, which represent the

corresponding motor neurons of the somatic segmentation and supply in this region only dorso-ventral muscles. It is a great mistake to call this bundle of motor fibres the descending root of the trigeminal without adding the word motor ; the right distinction between the two sets of trigeminal fibres called at present the " descending " and " ascending " roots is " descending motor " and " descending sensory " roots ; for the latter root behaves with respect to the somatic segmentation in exactly the same manner as the fasciculus solitarius, which is called the descending root of the vagus, with respect to the splanchnic segmentation.

Similarly, in the mesosomatic region (Fig. 1) the groups of motor cells, known as the facial nucleus and the nucleus ambiguus, represent the motor neurons of the splanchnic segmentation, and represent therefore the motor neurons of the muscles of the mesosomatic appendages ; they are quite separate from the nucleus of the abducens, which supplies motor fibres to the only remaining dorso-ventral muscles, a pair of which originally existed in each segment, and from the hypoglossal nucleus containing the motor cells of the longitudinal somatic muscles. These mesosomatic groups also extend down the cord ; the splanchnic group being represented by the nucleus accessorius or the lateral horn of the cervical region, which is formed from the lateral cell groups of the anterior horn ; the somatic group by the cells of the anterior horn, supplying motor fibres to the longitudinal trunk muscles.

Thus the cells of the motor neurons of the voluntary system form two well-defined groups in accordance with the double segmentation of the striated musculature in the cranial region.

On the sensory side (Fig. 1) there are also two distinct sets of sensory fibres represented in the double segmentation, belonging respectively to the somatic and splanchnic segments. In the prosomatic region the sensory neurons for both segmentations are found in the Gasserian ganglion ; but in the mesosomatic region the somatic sensory neurons belong mainly to the trigeminal and are also found in the Gasserian ganglion, while the splanchnic sensory neurons are found in the sensory ganglia on the facial, glossopharyngeal, and vagus nerves. So also there must be corresponding connector neurons for these two sets of segments, in order to carry out the primary or segmental reflexes, similar to those in the trunk region. These primary connector neurons are

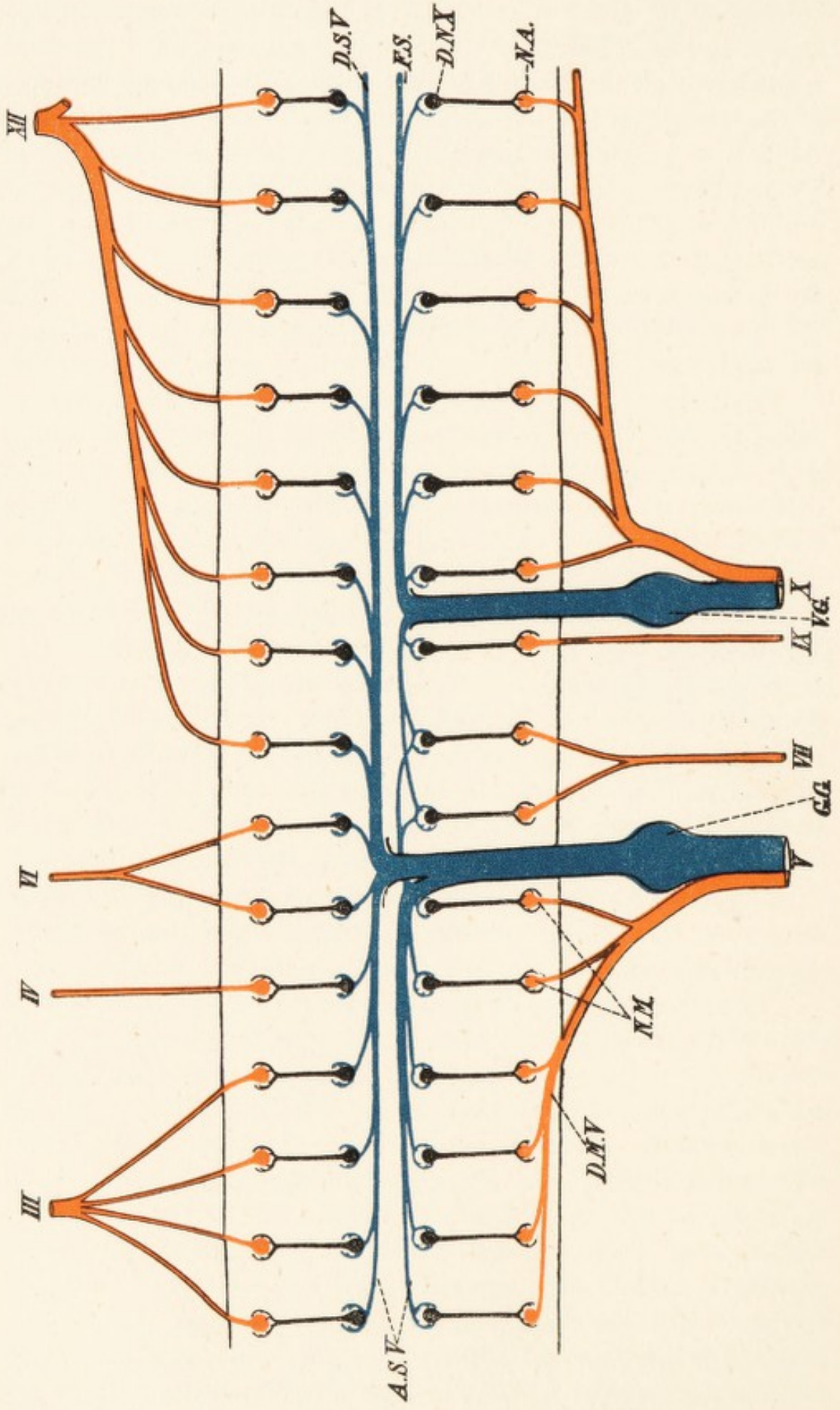

D.S.V
E.S.
D.M.X
N.A.
XII
X
Vg.
XI
VII
Gg.
V
VI
IV
III
N.M.
D.M.V
A.S.V

FIG. 1.—THE REFLEX PATHS OF THE VOLUNTARY SYSTEM IN THE CRANIAL REGION.

The afferent receptor neurons are shown in blue, the connector neurons in black, the efferent excitor neurons in red. This scheme of colouring holds for all the figures in this book.

The splanchnic excitor neurons are shown in the lower part of the diagram; the somatic excitor neurons in the upper part. The receptor neurons for both systems all run in the fifth and tenth nerves which are shown in the lower part of the diagram.

The neurons in a vertical line all belong to the same segment, the first six lie in the prosomatic segments, and the remainder in the mesosomatic.

The receptor fibres of the somatic system all run in the fifth nerve, their nuclei lying in the Gasserian ganglion, *G.G.*

The ascending sensory root, *A.S.V.*, supplies the connector neurons of the prosomatic segments of the somatic system. These connector neurons, which lie close against the ascending root, communicate with the excitor neurons of the four segments comprising the nucleus of the third nerve, with the nucleus of the fourth nerve, and with the anterior portion of the nucleus of the sixth nerve in the respective segments. The descending sensory root, *D.S.V.*, communicates with the connector neurons of the mesosomatic segments of the somatic system. The connector neurons connect in the first mesosomatic segment with the more posterior portion of the excitor nucleus of the sixth nerve and the others with the series of nuclei which form the excitor nucleus of the twelfth nerve.

The receptor fibres of the splanchnic system in the prosomatic region all run in the fifth nerve. They form part of the ascending sensory root and connect in each segment with connector neurons which in their turn connect with the nuclei of the descending motor root of the nerve, *D.M.V.* The nuclei of the two posterior segments form the nucleus masticatorius, *N.M.* Some afferent fibres of the fifth nerve probably connect also with the connector neurons of the seventh nerve as shown in the diagram.

The afferent fibres of the mesosomatic segments of the splanchnic system all run in the sensory portion of the tenth nerve, their cells lying in the vagus ganglion, *V.G.*

A small ascending root connects with the connector neurons of the first three segments; the connector neurons in their turn connect with the motor nuclei, the first two of which give origin to the seventh nerve and the third to the ninth nerve.

The descending root, the fasciculus solitarius, *F.S.*, connects with the connector neurons of the remaining segments which lie in the dorsal nucleus of the vagus, *D.N.X.* The motor neurons of these segments form the motor portion of the tenth nerve, the segmental nuclei lying in the nucleus ambiguus, *N.A.*

situated in the spinal region in the posterior horns (Fig. 2, A). We must look for the corresponding cells in the cranial region in two situations corresponding respectively to the posterior horns belonging to the somatic and splanchnic segmentations. The posterior horn cells of the cord are characterized by the presence of the substantia gelatinosa Rolandi close to them, and the characteristic of the descending sensory root of the trigeminal (Fig. 3, A) is the presence of the substantia gelatinosa Rolandi along its whole length. In this substance are found cells with which the fibres of this root continuously make connexion, called by Edinger the end nucleus of the "ascending" root. Such cells clearly correspond to a series of connector nuclei of the same kind as those belonging to the voluntary nervous system in the segments of the spinal cord, and form in my opinion the primary connector neurons of the somatic segmentation. I imagine therefore that, as far as the somatic segmentation is concerned, the primary or segmental reflexes, which must take place in each cranial segment as well as in each spinal one, are effected through these connector neurons, as represented diagrammatically in Fig. 3, A. With respect to the splanchnic segmentation (Fig. 3, B) in which the motor neurons are found in the nucleus of the facial, nucleus ambiguus and the accessory nucleus, and the sensory neurons in the ganglia on the roots of the corresponding nerves, we must look for the connector neurons in that part of the grey matter of the medulla oblongata which continues into the spinal cord as the posterior horn.

The posterior horn cells belonging to the vagus segments in the medulla oblongata have become part of the mass of cells in the floor of the fourth ventricle, known as the dorsal nucleus of the vagus, and according to Edinger the sensory roots of the vagus terminate in many of these cells and in their continuation as a cell column close along the "descending" root of the vagus (the fasciculus solitarius). In fact this group of cells forms the connector neurons belonging to the splanchnic segmentation in exactly the same manner as the corresponding group of cells in connexion with the sensory trigeminal fibres form the connector neurons belonging to the somatic segmentation.

I imagine therefore that, so far as the splanchnic segmentation is concerned, the primary or segmental reflexes, which must take place in each cranial segment as well as in each spinal one, are

effected through these connector neurons, as represented diagrammatically in Fig. 3, B.

Further consideration of the cells constituting the dorsal nucleus of the vagus is given in Chapter IX.

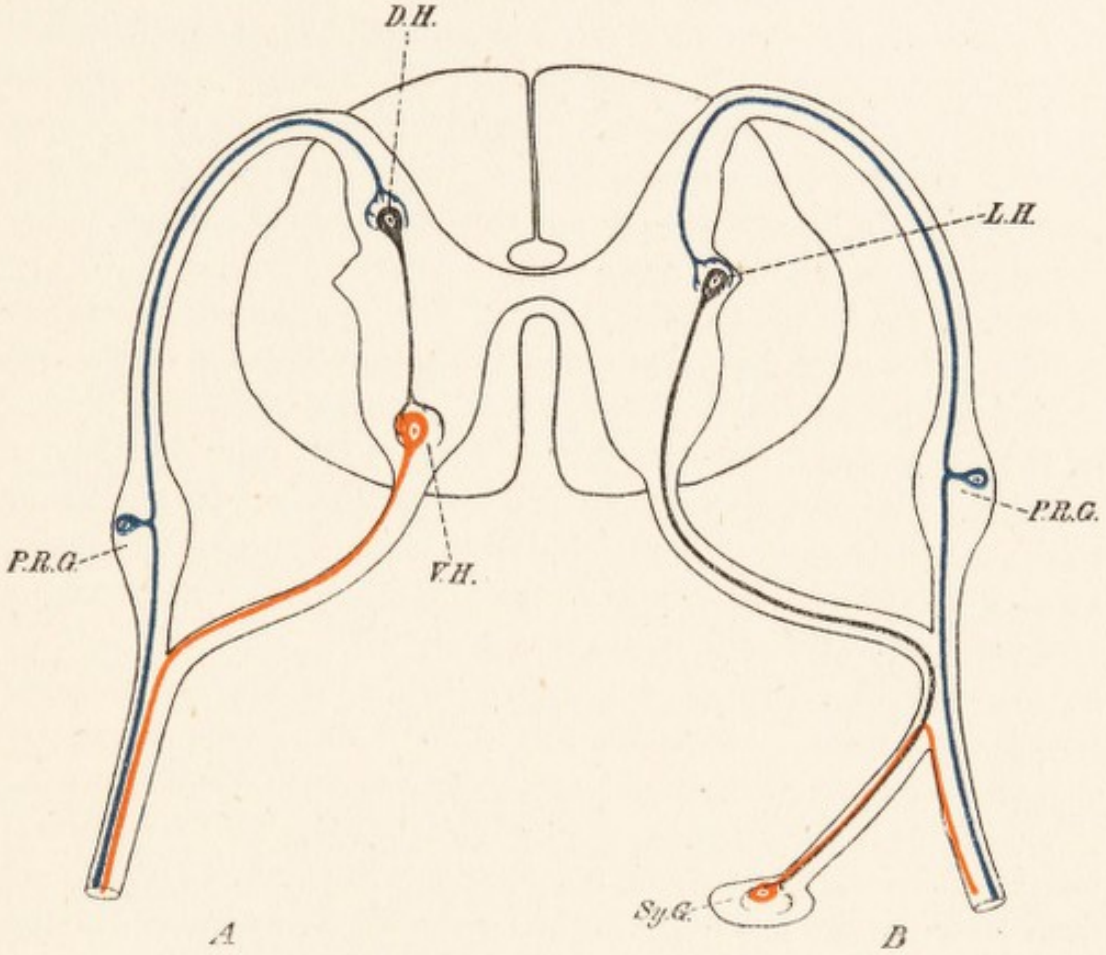


FIG. 2.—THE REFLEX PATHS IN THE CORD.

A. Of the voluntary system.

The receptor neurons run in the posterior root, their cells lying in the posterior root ganglion, *P.R.G.* The connector neurons lie in the dorsal horn, *D.H.*, and connect with the excitor neurons lying in the ventral horn, *V.H.*, whose processes run in the anterior root.

B. Of the involuntary system.

The receptor neurons run in the posterior root, their cells lying in the posterior root ganglion, *P.R.G.* The connector neurons lie in the lateral horn, *L.H.*, their processes running out in the anterior root and connecting, as the white ramus communicans, with the excitor neurons lying in the sympathetic ganglia, *Sy.G.* The processes of the excitor neurons form the grey ramus communicans and run out in the spinal nerve.

Turning now to the consideration of the involuntary nervous system, can we classify its muscles into morphological groups as in the case of the muscles of the voluntary system, and can we define with equal precision the position of its receptor, connector,

and excitor elements, with their sensory cells and sensory fibres, their intermediary cells and connector fibres and their motor cells and motor fibres? This book is an attempt to do so, and to put the involuntary nervous system on the same footing as the voluntary system. I propose to trace out the history of this involuntary system and show how our conceptions have been modified from time to time, to give our present knowledge, physiological and anatomical, of the different motor neurons of the system, and to give the evidence upon which it is possible to suggest the reason why the motor neurons of the involuntary tissues of the vertebrate have come to occupy their present position.

I will begin with the history of the sympathetic nervous system. The striking point about the sympathetic nerve, which distinguished it from all other nerves in the eyes of anatomists in the early days, was the presence of little knots or ganglia along the whole of its course; and as these could be traced up to the cranial region they concluded that the sympathetic nerve arose from the cranial region in the neighbourhood of the vagus and passed down to the end of the body.

Against this view of the cranial origin of the sympathetic nerve Petit urged that stimulation of the cervical sympathetic caused dilatation of the pupil, and Winslow pointed out that the branches from the superior cervical ganglion towards the cranial nerves diminished in calibre, a fact which was not in accordance with their origin from the cranial nerves. He considered the ganglia to be scattered centres of origin of the sympathetic system and called them the little brains of that system.

Haller's discovery of the existence of communications between the ganglia and all the spinal nerves, to which he gave the name "*rami communicantes*," threw an absolutely new light on the sympathetic system and has been the basis of all subsequent investigations.

Of all those in the past whose influence has produced most effect upon our conceptions of the sympathetic system, the name of Bichât comes prominently forward. He taught that two great systems existed in every vertebrate, the one concerned with the outside world, represented by the organs of locomotion and external sense-organs, to which he gave the name animalic; the other concerned with the regulation of the nutrition of the body, to which he gave the name organic. Each of these systems had

its own central nervous system, the cerebro-spinal regulating the animalic, and the sympathetic ganglia the organic systems respectively. So fascinating was this conception and so enthusiastically was it received, that closer comparisons between the

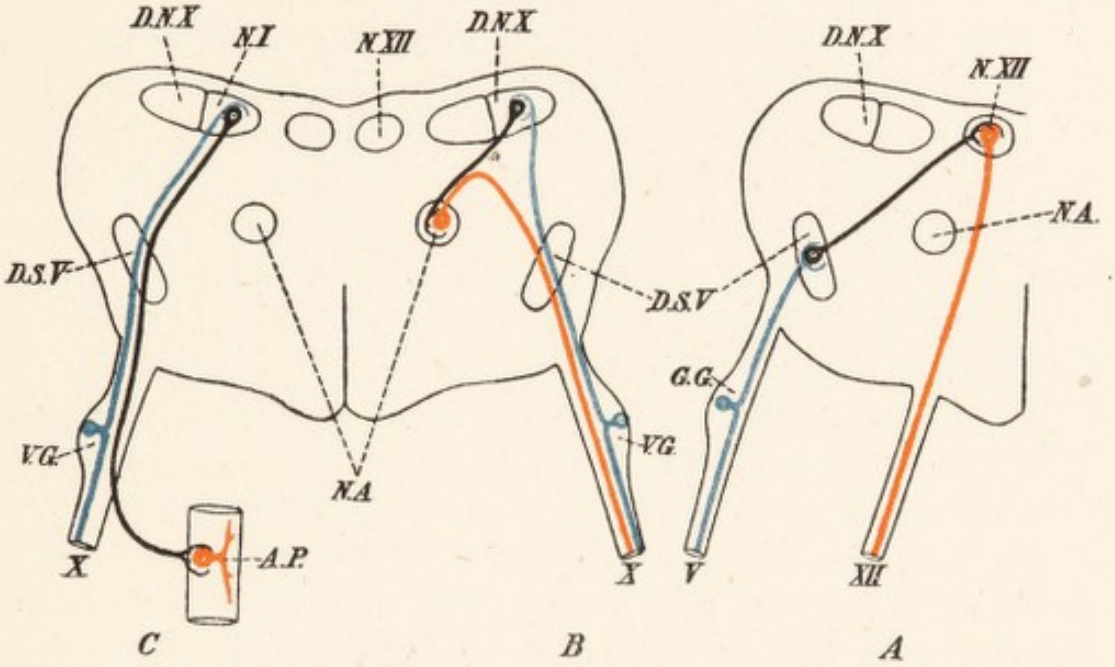


FIG. 3.—THE REFLEX PATHS IN THE BULBAR REGION.

A. Of the somatic system.

The afferent neurons run in the fifth nerve, *V.*, their cells lying in the Gasserian ganglion, *G.G.* These connect with the connector neurons lying close against the descending root of the fifth nerve, *D.S.V.* The connector neurons in their turn connect with the excitor cells which lie in the nucleus of the twelfth nerve, *N.XII.*

B. Of the splanchnic system.

The receptor neurons run in the tenth nerve, *X.*, with their cells lying in the ganglion of this nerve, *V.G.*, and connect with connector neurons which lie in the dorsal nucleus of the vagus, *D.N.X.* Processes of the connector cells connect with the excitor neurons which lie in the nucleus ambiguus, *N.A.*, their processes form the motor part of the tenth nerve.

C. Of the involuntary system.

The receptor neurons run in the tenth nerve, *X.*, with their cells in the ganglion of this nerve, *V.G.*, and connect with connector neurons which lie in the nucleus intercalatus of Staderini, *N.I.*, which forms a part of the dorsal nucleus of the vagus, *D.N.X.* The processes of these connector neurons run out in the vagus nerve, *X.*, and finally connect with the excitor neuron which lies on some peripheral organ, e.g. in the case of the intestine lying in Auerbach's plexus, *A.P.*

two systems were made by subsequent writers; thus the main sympathetic chain was compared to the spinal cord and the ganglion cœliacum (solar ganglion) was looked upon as the head centre or brain of the organic system, by its position emphasizing as strongly as possible the conception that the sympathetic system

was essentially a system concerned with the innervation of the alimentary canal and its glands.

Following upon this separation of the two central nervous systems came the separation of the nerve fibres belonging to them, consequent upon the discovery by Remak of non-medullated fibres which belonged entirely to the sympathetic system; later Joh. Müller, taking into consideration the fact that the rami communicantes were partly grey and partly white, put forward the proposition that the white fibres were cerebro-spinal and the grey sympathetic, so that there was a reciprocal connexion between the two nervous systems, the animalic centres sending animalic fibres to the organic centres, which in their turn sent organic fibres to the animalic centres.

Thus Bichât's teaching appeared to be based on the strongest possible foundations of fact, and the absolute independence of the animalic and organic nervous systems established.

Furthermore the very conception of this separate organic system, together with the position of its main mass in the solar ganglia, firmly inculcated the view that the sympathetic system was essentially connected with the viscera, and even to this day comparative anatomists, on the discovery of nerves going to the intestines of some invertebrate animal, frequently describe them as representing the sympathetic nerves in such an animal. A further extraordinary conception, which arose out of the teaching of the absolute independence of this organic system, and was held somewhat largely, and taught by some anatomists when I began my medical studies, was that the sympathetic system represented the central nervous system of such invertebrates as insects and that the cerebro-spinal system was superadded, being special to the vertebrate.

Bichât's views were largely prevalent when I took up the question and determined to settle whether there was a reciprocal communication between the two systems. For this purpose I cut serial sections through the rami communicantes and through the roots of the spinal segmental nerve after treatment with osmic acid, and found, as was well known, that the main mass of the non-medullated fibres, after entering the spinal segmental nerve, turned peripheral-wards along the nerve, but that a smaller number proceeded along the roots towards the spinal cord. On tracing these latter, which especially went along the posterior root, they

were found to pass off into the membranes round the spinal cord to supply the blood vessels: none entered into the spinal cord itself. It was perfectly evident that the reciprocal connexion between the two nervous systems did not exist, that in fact all the characteristic sympathetic nerve fibres—non-medullated fibres—wherever found are peripheral nerves; and incidentally an observation of Valentine "that stimulation of posterior roots caused constriction of the blood vessels of the dura mater" was explained.

At the time when I made these observations, I was unaware that Beck had published a paper in the "Philosophical Transactions" in 1846, in which he gave evidence for the suggestion that all the non-medullated fibres passing in towards the spinal cord were peripheral fibres.

Further, if there were two distinct nervous systems, animalic and organic, the one forming a peripheral nervous system and the other a central nervous system, there must be a separate origin for these two systems. At about the same time Onodi showed that each of the groups of cells, which form collectively the main chain of the sympathetic system, had differentiated out from a mass of cells close against the central nervous system, and that the remainder of this mass formed the posterior root ganglion. These observations of Onodi point to the conclusion that the ganglia of the sympathetic chain do not arise independently, but are originally a part of the central nervous system, and have emigrated still further than the ganglia of the posterior roots.

The observations of Onodi, of Beck, and myself gave the death-blow to Bichât's conceptions of the independence of the sympathetic nervous system, and proved that there is only one system of communication between the organic and animalic nervous systems, viz. the white rami communicantes.

The next step was to trace the white rami communicantes into the spinal cord. Sections of osmic preparations of the white rami of the second thoracic nerve showed that its structure was very different from that of ordinary nerves, in that it was composed almost entirely of very small medullated fibres. On examining the roots of that nerve, masses of similar fine medullated fibres were found in the anterior root.

I then proceeded to cut sections of the anterior roots of all the spinal nerves, and discovered that these masses of small

medullated fibres were not uniformly present. They were most prominent in the second and following thoracic roots, and were found in the anterior roots throughout the whole thoracic region and the beginning of the lumbar region. I found, as naturally was to be expected, that they corresponded to the region of white rami communicantes ; above and below this region there are only grey rami communicantes ; the white are absent. This peculiarity of the anterior roots in the thoracic region had been noticed by Reissner, but he could not explain it.

These observations showed that the central nervous system supplies efferent fibres in the white rami communicantes to the main sympathetic chain only in the thoracico-lumbar region.

The next question was to find out the relation between the fine white medullated cerebro-spinal fibres and the grey non-medullated sympathetic fibres. I argued as follows: the accelerator nerves to the heart from the ganglion stellatum and inferior cervical ganglion are clearly non-medullated ; stimulation of the second and third roots in the thoracic region cause acceleration ; these accelerator fibres pass to the ganglion stellatum along the rami communicantes and are medullated right up to the ganglion ; the conclusion is that the medullated fibres, which cause acceleration, end in sympathetic cells in the ganglion, and that these cells give origin to the non-medullated accelerator fibres which pass to the heart. I argued similarly with respect to the whole group of vaso-constrictor nerves, which also leave the spinal cord as fine medullated nerves and pass to the blood vessels from sympathetic cells as non-medullated fibres. The conclusion then to which I came in 1885 was that the sympathetic cells consisted largely, if not entirely, of a system of motor cells situated on the path of efferent fibres from the cord to the peripheral organ ; that in fact both roots might be looked upon as ganglionated, the anterior as well as the posterior. With the coming in of the neuron theory, and the conception of a series of relays in the nervous system, it is held that these motor cells represent the terminal neurons of the efferent system, just as the sensory cells of the posterior root ganglia represent the terminal neurons of the afferent system ; the difference between the two sets being the fixed position of the latter on the posterior roots just near the spinal cord, and the vagrant character of the former at various distances from the cord.

These conclusions as to the relation of the sympathetic nerve cells to the fibres of the white rami communicantes were confirmed by Langley and Dickinson in 1889 in consequence of observations upon the action of nicotine; for they showed that the injection of nicotine prevented the effect of stimulation of the fibres from the spinal cord which go to the sympathetic ganglia, i.e. the ramus communicans, but did not affect the fibres from the sympathetic ganglia. In other words, the action of the nicotine upon the sympathetic cell or upon the junction of the spinal fibre and the sympathetic cell prevented the action of the latter fibres.

These spinal fibres Langley named "pre-ganglionic," and the sympathetic fibres "post-ganglionic."

There are two distinct groups of ganglia belonging to this system, in the first place a chain of ganglia lying along the vertebrae on each side, the vertebral or lateral ganglionic chain, and in the second place, ganglionic masses lying on each side of the abdominal aorta which form the prevertebral or collateral ganglia. These latter form two principal groups of ganglia, the largest and most anterior forming a mass round the cœliac axis which is often called the solar ganglion.

This mass is divisible into two parts, the semilunar ganglia and the superior mesenteric ganglia. The sympathetic fibres arising from the cells of the semilunar ganglia pass with the blood vessels to the stomach, liver and spleen, and those from the cells of the superior mesenteric ganglia run with the branches of the superior mesenteric artery, and are therefore concerned with the innervation of the small intestine and its blood vessels. In addition to the superior mesenteric and semilunar ganglia there is also a small ganglion found on each side, the renal ganglion, which supplies the kidney with sympathetic fibres.

The smaller posterior group forms a ganglionic mass which bears the same relation to the inferior mesenteric artery as the larger mass does to the superior mesenteric, and its sympathetic fibres pass to the periphery with the branches of the inferior mesenteric artery; they are concerned with the innervation of the large intestine and its blood vessels.

Between the inferior and superior mesenteric ganglia a small ganglion is found on the walls of the aorta—the ovarian or spermatic ganglion—the fibres from which pass to the ovaries or testis by way of the ovarian or spermatic artery respectively.

All these collateral ganglionic masses are connected with the central nervous system by means of the splanchnic nerves. It was once thought that, just as the rami communicantes connected the central nervous system with the ganglia of the lateral chain, so the splanchnics connected the ganglia of the lateral chain with the collateral ganglionic masses. Milne Edwards gave the name rami efferentes to the whole set of nerves, which were held to connect these two groups. There is, however, in reality no such connexion, the splanchnic nerves are simply rami communicantes direct from the central nervous system to the cells of the collateral chain, the fibres of which lie along the lateral or main chain for part of their course and so appear to spring from the ganglia of that chain.

The splanchnic nerves are divided into two very distinct groups, an upper or superior group, which contains the largest nerve—the splanchnic nerve proper—and connects with the superior mesenteric, semilunar, and renal ganglia, and a lower or inferior group, consisting of three to four nerves which connect with the inferior mesenteric ganglion. The whole set may be called the abdominal splanchnic nerves, and in consideration of their relation to the roots of the spinal cord it is often convenient to speak of the superior group as the thoracic splanchnics and of the inferior group as the lumbar splanchnics.

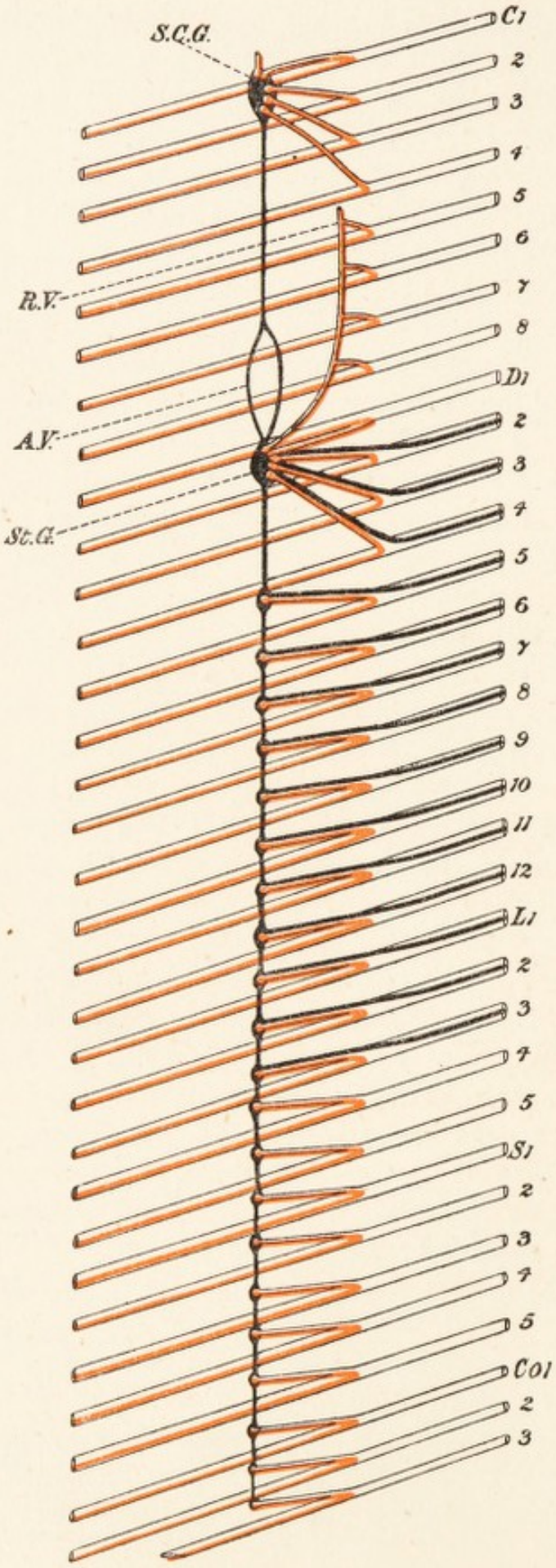
The lateral ganglia (Fig. 4) form a segmentally arranged chain corresponding to the segmental spinal nerves, each ganglion sending sympathetic fibres to its corresponding nerve and to its corresponding spinal segment. The upper ganglia in the thoracic region have become fused to form the large ganglion stellatum; and the ganglia of the cervical region have fused to form the inferior and superior cervical ganglia, the latter of which supplies the three foremost cervical nerves, the rest being supplied by sympathetic fibres from the inferior cervical ganglion and from the ramus vertebralis, a striking grey ramus from the ganglion stellatum, which supplies the four lower cervical nerves and corresponding spinal segments.

The evidence up to this point is clear, that the so-called sympathetic system consists of an outflow from the spinal cord of fine medullated efferent nerves, which terminate in or around nerve cells, whose fibres (sympathetic or post-ganglionic) proceed to and supply the peripheral organs. Although I was strongly

of opinion that all these vagrant sympathetic ganglia gave origin to efferent nerve fibres and none of them to afferent, I did not attempt to decide the question. Undoubtedly a certain number of the medullated fibres of the ramus communicans pass towards the cord into the posterior root ganglion and so into the posterior roots, the proportion of these to the motor fibres in the same ramus differing largely in different nerves. Thus the white rami which form the nervus erigens contain, according to Langley and Anderson, as many as $\frac{1}{3}$ afferent fibres and only $\frac{2}{3}$ efferent, while in the hypogastric nerve the respective numbers are as 1 to 10.

Sections of the posterior roots however give no such striking picture as in the case of the anterior roots; for it is not possible to distinguish by differences of structure in the posterior roots the distribution of the white rami communicantes. Fine medullated fibres were much more universally to be found in all these roots, no matter where they were situated. Langley has, I think, settled this question definitely by the method of degeneration. If sensory cells exist in the lateral chain of ganglia, then sections of the ramus communicans, after time allowed for degeneration, must show the presence of degenerated fibres in the part still in connexion with the spinal nerves; and similarly sections of the "rami efferentes" should show the presence of degenerated fibres in their ends, which appear to spring from the lateral chain, if their nutrient centres were in cells of the collateral ganglia. In neither case is there any evidence of degeneration. All the afferent fibres have their nutrient centres in the posterior root ganglia. No peculiarity therefore exists on the afferent side; the course of the sensory fibres is the same in all sensory nerves, viz.: direct to the cells of the posterior root ganglia with no connexion with any cells in sympathetic ganglia. Seeing then that all the fibres entering into the posterior root ganglia are medullated, it follows that all non-medullated fibres are efferent, none afferent, and that the so-called sympathetic system is not a complete central nervous system, but consists purely of excitor neurons.

As already stated, these motor nerve cells and the sensory nerve cells at one period formed a single mass of cells in the position of the posterior root ganglion, and then, as growth went on, the motor or sympathetic mass separated off and became more and more vagrant, while the sensory mass remained stationary just outside the spinal cord. A reminiscence of the original state


S.C.G.
C1
2
3
4
5
6
R.V.
7
8
D1
A.V.
2
3
4
St.G.
5
6
7
8
9
10
11
12
L1
2
3
4
5
S1
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4
5
Co1
2
3

FIG. 4.—THE ARRANGEMENT OF THE CONNECTOR FIBRES (BLACK) AND THE EXCITOR NEURONS (RED) OF THE SYMPATHETIC SYSTEM IN THE SPINAL REGION.

All the spinal nerves are shown from the first cervical, *C.*1, to the third coccygeal, *Co.*3.

All the connector neurons leave the spinal cord in the thoracico-lumbar outflow which extends from the second dorsal, *D.*2, to the third lumbar, *L.*3. The lateral chain of sympathetic ganglia is connected together by the further prolongation of these processes which run from ganglion to ganglion, connecting in three or more of them with the cells of excitor neurons. The lateral chain is therefore made up of a series of groups of excitor neurons connected together by the processes of connector neurons. Certain ganglia have become fused, those corresponding to the first four cervical nerves being aggregated into superior cervical ganglion, *S.C.G.*, those of the last four cervical and the first four dorsal being aggregated into the stellate ganglion, *St.G.*, which lies just caudal to the annulus of Vieussens, *A.V.* For the sake of simplicity the ganglia on this annulus and the inferior cervical ganglion have been omitted and considered part of the stellate ganglion. The processes of the excitor neurons belonging to any ganglion run out in the grey ramus communicans to join the spinal nerve and to be distributed with it. The excitor fibres for the first four cervical nerves thus arise from the superior cervical ganglion, *S.C.G.*; the excitor neurons for the last four cervical nerves arise from the stellate ganglion, *St.G.*, and at first all run in the ramus vertebralis, *R.V.*, they finally branch from this and join their respective nerves. Similarly the excitor fibres of the first four dorsal nerves all arise from the stellate ganglion, *St.G.*, to which the first three white rami communicantes run. The rest of the spinal nerves are supplied with sympathetic excitor fibres from their corresponding sympathetic ganglia.

of things is seen in the young crocodile, where the rami communicantes between the nerve and the ganglionic chain are very short, so that the posterior root ganglion is very near the corresponding sympathetic ganglion, and in the tortoise, where the ramus communicans in the thoracic region springs directly out of the posterior root ganglion. According to Giacomini in Bufo and Bombinator the two ganglia actually touch one another.

This fact, that the sympathetic system of cells has split off from a cell mass in the position of the posterior root ganglion, has led many anatomists to look upon the sympathetic ganglia as offshoots of the posterior root ganglia, and therefore mainly sensory in function. Langley's evidence makes it clear that it is only the motor cells which have passed peripheral-wards, while the sensory cells of the system have remained in their original position in the ganglion of the posterior root.

Further, those who hold that the sympathetic system is an independent nervous system, not only find a necessity for the presence of sensory cells in that system, but also consider that the cells of the different ganglia are connected together, thus forming a system of relays, as in the central nervous system. Acting on the principle that a nerve cell keeps alive that part of the nerve fibre which is in connexion with it, Langley argued that, after section of the spinal roots and after time had been allowed for degeneration of their peripheral ends, stimulation of the splanchnic nerves (rami efferentes) ought still to produce an effect, if the cells of the lateral chain communicated with cells of the collateral chain. He, however, found no effect under these conditions; there is therefore no commissural system between these two sets of sympathetic ganglia. Similarly he showed that the cells in separate ganglia of the vertebral chain do not connect with each other. Therefore this characteristic of relays of cells which connect with each other, which is so important a factor in the making of a central nervous system, is not to be found in the sympathetic nervous system.

I have made use hitherto of the term organic system in accordance with old usages to represent in part the nerve cells and nerve fibres of this thoracico-lumbar outflow; but this term is so bound up with the ideas of the independence of the organic and animalic systems—an objection which applies on the face of it also to Langley's substitution of "autonomic" for organic—that

it is no longer suitable. So far as the term system can be used at all, we are dealing only with motor cells and motor nerves to a special set of tissues, and with the connexions of such motor neurons with the central nervous system. There is one characteristic common to these special tissues, they are not directly under the command of the will. The motor nerve cells in question invariably send motor nerve fibres to involuntary muscles or glands, just as the motor nerve cells in the central nervous system send motor nerve fibres to voluntary muscles. The natural term then to use, if we wish to group together these vagrant motor cells and their connexions into one system, is to speak of it as the involuntary nervous system in contradistinction to the voluntary nervous system ; meaning thereby a system of motor nerve cells to involuntary structures, which have left the central nervous system and have migrated out to a greater or lesser distance.

Now the vertebrate body is undoubtedly segmented ; that segmentation is shown on the motor side by the segmentation of the body muscles in the trunk region to form the myotomes, and by their innervation by the motor nerves, which pass from the anterior horn cells into each spinal nerve ; again on the sensory side it is shown by the presence of the posterior root ganglion in each segment and the distribution of its sensory nerves to a definite segmental skin area. Each spinal nerve then is a segmental nerve as far as concerns the central and peripheral distribution of its motor and sensory components. We may then inquire how far such an arrangement also obtains in the case of its sympathetic components. The motor fibres which supply the muscles of the involuntary system arise from the vagrant ganglion cells of that system, and in the case of the so-called sympathetic part of that system, form the grey rami communicantes. These grey rami from each of the ganglia of the lateral or main chain supply the corresponding spinal nerve, and, as Langley has shown in the case of the pilo-motor muscles, reach their destination by way of the cutaneous branches of that nerve ; they thus afford evidence that these segmentally arranged motor neurons are closely associated in the adult with the segmental cutaneous sensory neurons, which must be the case if they have separated out from a conjoined mass of sensory and motor neurons, as Onodi has shown. Here then in the lateral ganglia of the sympathetic chain we find the true segmental motor nerve

cells of these involuntary muscles, and the motor fibres from these cells are the true homologues of the motor fibres to the voluntary muscles. How then are we to look upon the fibres from the spinal cord which connect these cells with the central nervous system, the white rami communicantes? If it be a true way of looking at the main chain of the sympathetic system, that it consists of groups of motor cells arranged segmentally, which give origin to the motor fibres of a special group of muscles and were originally in the central nervous system, then it follows that the connexions between the central nervous system and such cell groups, the white rami communicantes, are not of the nature of motor nerves, but must be looked upon as efferent tracts connecting one part of the central nervous system with another; just as the optic nerve is not a sensory nerve but a nerve tract connecting two parts of the central nervous system. That this is the right way of looking at this system is made certain by Langley's observations on the innervation of the unstriped muscles which move the hairs of the skin; for he has shown that, whereas the stimulation of each grey ramus from each sympathetic ganglion of the main chain causes a movement of hairs over the same segmental area of skin as is supplied by the sensory nerves of the corresponding posterior root ganglion, the stimulation of the connecting fibres in the corresponding anterior root—that is to say the pre-ganglionic fibres of the ramus communicans—causes a movement of hairs over a large number of such segmental areas. Further, he has given reasons for the belief that this effect is due to the fact that these pre-ganglionic fibres do not connect with the cells of only one ganglion, but each fibre sends off collaterals and thus connects with many of the segmental ganglia. In other words, these fibres of the rami communicantes, like the fibres of the pyramidal tracts, connect with the motor cells of many segments by means of collaterals, and are connector, not motor, fibres.

The distribution of the motor nerves of the sympathetic system manifests therefore a segmental arrangement of the same kind as that of the motor nerves of the voluntary muscles; but the anterior roots of the spinal nerves are not, as in the case of the voluntary system, the manifestation of that segmental arrangement; for they contain, not the motor fibres of the sympathetic musculature, but the connector fibres to the segmentally

arranged motor neurons of that musculature, and the fibres in each anterior root make connexion with the motor neurons of many segments (Fig. 2, B).

Everything therefore points to the conclusion that the so-called sympathetic nervous system consists simply of masses of motor neurons to a special system of muscles, which have left the central nervous system, but are still connected with it by connector fibres in the rami communicantes. By the term motor, I include true motor nerves, nerves inhibitory to muscular movements, and glandular nerves. The connector fibres are confined to a limited portion of the spinal cord and constitute the thoracico-lumbar outflow. There are in fact two sets of connector fibres, the one belonging to the involuntary system, which remains in the central nervous system, and the other belonging to the involuntary system, which passes out from the central nervous system in the rami communicantes, to connect with the motor neurons of the involuntary system.

The study of the evolution of the animal kingdom, as I have pointed out in the "Origin of Vertebrates," brings out prominently the enormous importance of the development of the central nervous system in the upward progress of the race: in the struggle for existence, such progress must necessarily be associated with the greater development of the voluntary part of the nervous system. The whole history of the progressive evolution of the vertebrate animal up to its culmination in man is evidence of the steady growth in bulk and complexity of that part of the central nervous system which is associated with voluntary movements; it is the growth of will power, with all that that implies, which has led to the domination of man over the rest of the animal kingdom. Such growth of the voluntary nervous system necessitates increase in bulk and concentration; and so has brought about the large size of the brain. Such being the lines on which evolution has proceeded, it stands to reason that the more this concentrated voluntary system is freed from the subordinate involuntary system consistently with the continuance of the harmonious interaction between the two systems, the greater will be the advantage to the animal. This is what embryology teaches: the motor cells of the involuntary nervous system originally formed part of the central nervous system, and by their migration towards the peripheral organs freed the central nervous system from a very large

mass of nervous material, and so enabled a more efficient concentration of the elements of the voluntary nervous system. At the same time the involuntary connector fibres, which form the efferent part of the rami communicantes, were sufficient to maintain the necessary efficiency of the interaction between the central nervous system and the motor cells of the involuntary system, taking into consideration the nature of the movements of involuntary muscle. These movements are essentially movements *en masse* and not delicately co-ordinated movements, such as are so characteristic of the voluntary system ; indeed, the evidence shows that movements of the involuntary system of muscles, brought about reflexly through the central nervous system, always involve a large number of muscle fibres. This must be the case when we consider that each single fibre that leaves the central nervous system can activate by means of collaterals many motor nerve cells, each of which in its turn innervates many muscle fibres.

The limits of the outflow of nerves from the spinal cord, which pass to the cells of the sympathetic ganglia (Fig. 4), are defined by the structure of the anterior roots and consequent presence or absence of a white ramus communicans. The upper limit is defined by the brachial plexus and the lower by the lumbo-sacral plexus.

The next question for consideration was whether there were similar outflows of fine medullated efferent fibres either below or above these limits. To settle this question I proceeded to cut sections of the anterior roots of all the spinal nerves, and found that again in the anterior roots of the second and third sacral nerves there was evidently another mass of these small medullated fibres. It was easy to follow these small fibres outwards into two separate nerves which joined together to form the nervus erigens ; that is to say, the structure of these roots demonstrates an outflow of fine medullated fibres from the spinal cord, to form a ramus communicans, not to any ganglia of the vertebral chain, but to separate sets of ganglia lying on the surface of the bladder and rectum (Fig. 5, P). These fibres pass directly to these ganglion cells without having anything to do with the lateral or main chain of sympathetic ganglia, just as the nerves, which form the splanchnics, pass direct to the collateral ganglia of the sympathetic independently of the lateral

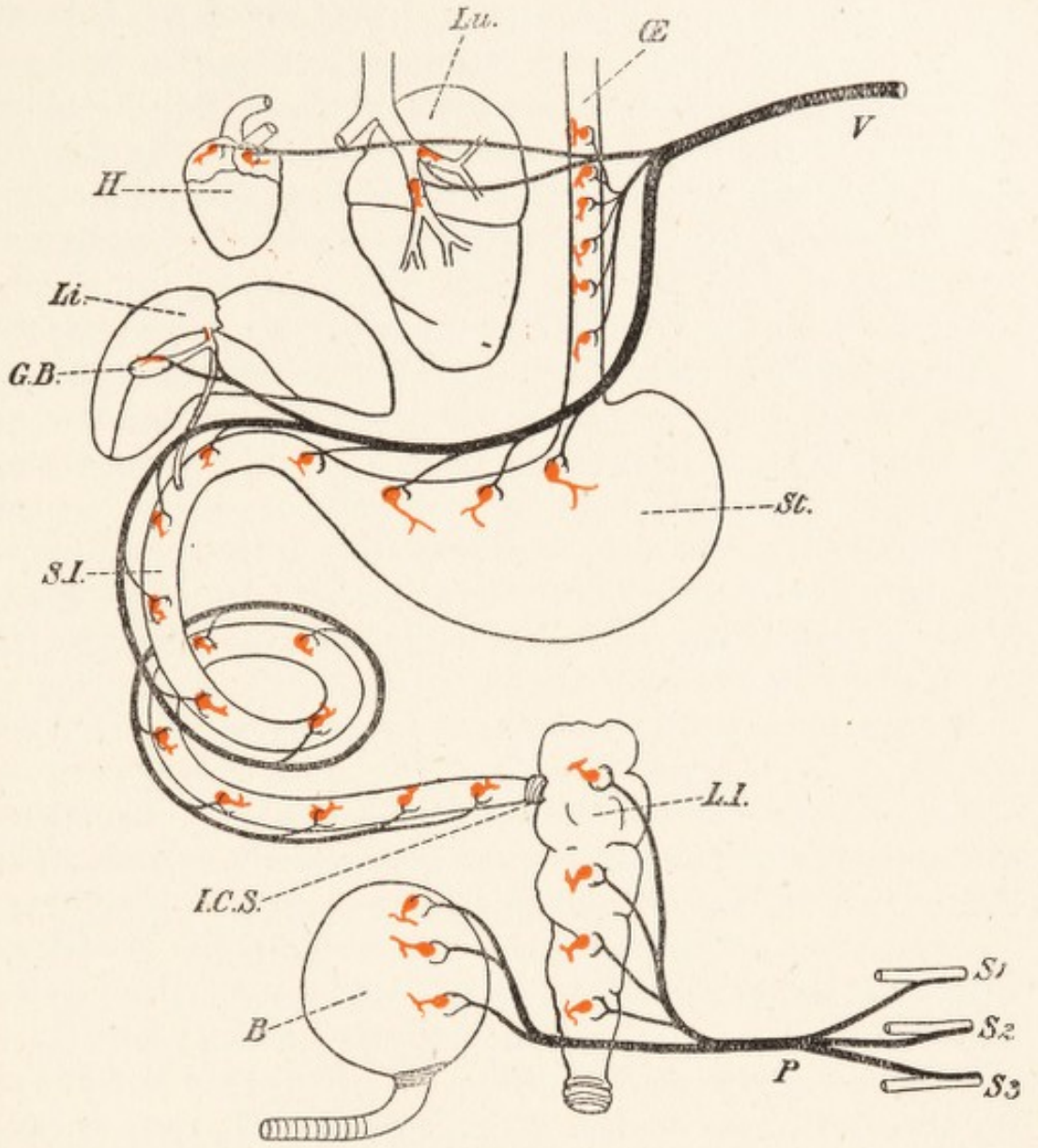


FIG. 5.—THE DISTRIBUTION OF THE CONNECTOR FIBRES (BLACK) AND EXCITOR NEURONS (RED) OF THE BULBO-SACRAL OR ENTERAL SYSTEM.

The vagus nerve, *V.*, contains the connector nerves of the excitor neurons of the main viscera as far as the ileo-colic sphincter, *I.C.S.* The motor neurons all lie on the organs themselves.

The pelvic nerve, *P.*, contains the connector fibres of the sacral outflow and connects with peripheral excitor neurons on the large intestine and bladder.

The vagus nerve thus contains the connector neurons to the motor cells of the heart, *H.*, which have to do with the slow wave-like contraction which is only found in certain tortoises, such as Emys Europœa, and does not appear to exist in higher forms. The vagus nerve also contains the connector fibres to the excitor neurons on the bronchi in the lung, *Lu.*, and also the connector fibres to the excitor neurons on the gall bladder and bile duct lying on the liver, *Li.*; it also contains the connector fibres to the excitor neurons of the œsophagus, *Œ.*, the stomach, *St.*, and the small intestine, *S.I.*, which here lie between the muscle layers in Auerbach's plexus.

The pelvic nerve, *P.*, which arises from the three sacral roots, *S.* 1, 2 and 3, contains the connector fibres to the excitor neurons of the large intestine, *L.I.*, and also the connector fibres of the excitor neurons of the body of the bladder, *B.*

or main chain of sympathetic ganglia. Evidently this sacral outflow of fine medullated nerves corresponds in position to those thoracico-lumbar rami communicantes, which are designated by the name of the abdominal splanchnic nerves, rather than to those which connect with cells of the main sympathetic chain. For this reason, and because the name *nervus erigens* only expresses a part of the functions of this sacral outflow, I originally called this nerve the *pelvic splanchnic* nerve. There are however many advantages in confining the use of the word splanchnic to fibres connected with cells of the sympathetic nervous system, so it is better to leave out the term splanchnic and call the *nervus erigens*, as Langley has done, the *pelvic nerve*.

Thus it is evident that there exist two distinct outflows of efferent fine medullated fibres from the spinal cord to motor ganglia outside it, the one limited to the thoracico-lumbar region and the other to the sacral region.

I then proceeded to examine the anterior roots above the thoracic region to see whether there was any evidence of groups of fine medullated fibres in them, and found no trace of anything of the kind in any of the anterior roots of the cervical nerves. But it must be remembered that in this region of the spinal cord there are three roots, not two, a dorsal root, a ventral root, and a lateral root. The system of lateral roots forms the spinal accessory nerve, a nerve which is distinctly motor in function ; I therefore cut sections of the roots of the spinal accessory and found in the uppermost roots distinct evidence of an outflow of very fine medullated fibres. Tracing these to their destination, I found that they all passed into the internal branch of the spinal accessory to join the vagus nerve, leaving the external branch, which is the nerve to the trapezius and sterno-cleido-mastoid muscles, free from admixture with such fine fibres. These upper rootlets of the spinal accessory pass imperceptibly into the rootlets of the vagus, adding more and more of the fine medullated fibres to that nerve, which is one of the main nerves of the organic system. Here then was evidence of a cranial outflow of nerve fibres of the same kind as those in the thoracico-lumbar and sacral regions. Further investigation showed that such nerves as the nervus tympanicus, running from the glossopharyngeal to the otic ganglion by way of the lesser superficial petrosal, the chorda tympani, running from the facial to the submaxillary

ganglion by way of the lingual nerve, and the great superficial petrosal, running from the facial to Meckel's ganglion, were all of the nature of rami communicantes in their composition (Fig. 6, B).

This cranial outflow of connector nerves is found in connexion with those segmental nerves which arise from the medulla oblongata, and may receive the name of the bulbar or mesosomatic outflow.

Anterior to the mesosomatic or bulbar region we come to the prosomatic region of the cranial segmental nerves, represented in the voluntary nervous system on the motor side by the nerves to the masticatory muscles and on the sensory side by the trigeminal nerves. Here again I found an outflow of fine medullated fibres in the roots of the oculomotor nerve separating out from the larger motor fibres to the striated ocular muscles to pass into the ciliary ganglion, from the cells of which nerve fibres arise to form the short ciliary nerves, which are motor to the sphincter muscle of the iris and the muscles of accommodation (Fig. 6, A). This outflow of connector nerves may receive the name of the prosomatic or mid-brain outflow.

Such was the fundamental conception of the involuntary nervous system which I gave in 1885 : three great outflows of fine medullated fibres to peripheral motor ganglion cells, from the bulbar, thoracico-lumbar, and sacral regions respectively, these three outflows being roughly separated from each other by the formation of the nerve plexuses for the upper and lower limbs ; and in addition a smaller separate outflow from the mid-brain region.

Just as Onodi showed that the peripheral nerve cells, with which the thoracico-lumbar outflow is connected—the so-called sympathetic cells—were originally in close contiguity with the cells of the posterior root ganglia of the spinal cord, and that they separated and became situated more and more peripherally during development; so Kuntz and Miss Abel have shown that the peripheral nerve cells belonging to the vagus system, with which the bulbar outflow is connected, were originally in close contiguity with the cells of the posterior root ganglia of the vagus group of nerves, and that they also separated and became situated more and more peripherally during development.

We may sum up the results of this chapter as follows. The evidence indicates that the involuntary nervous system is built up

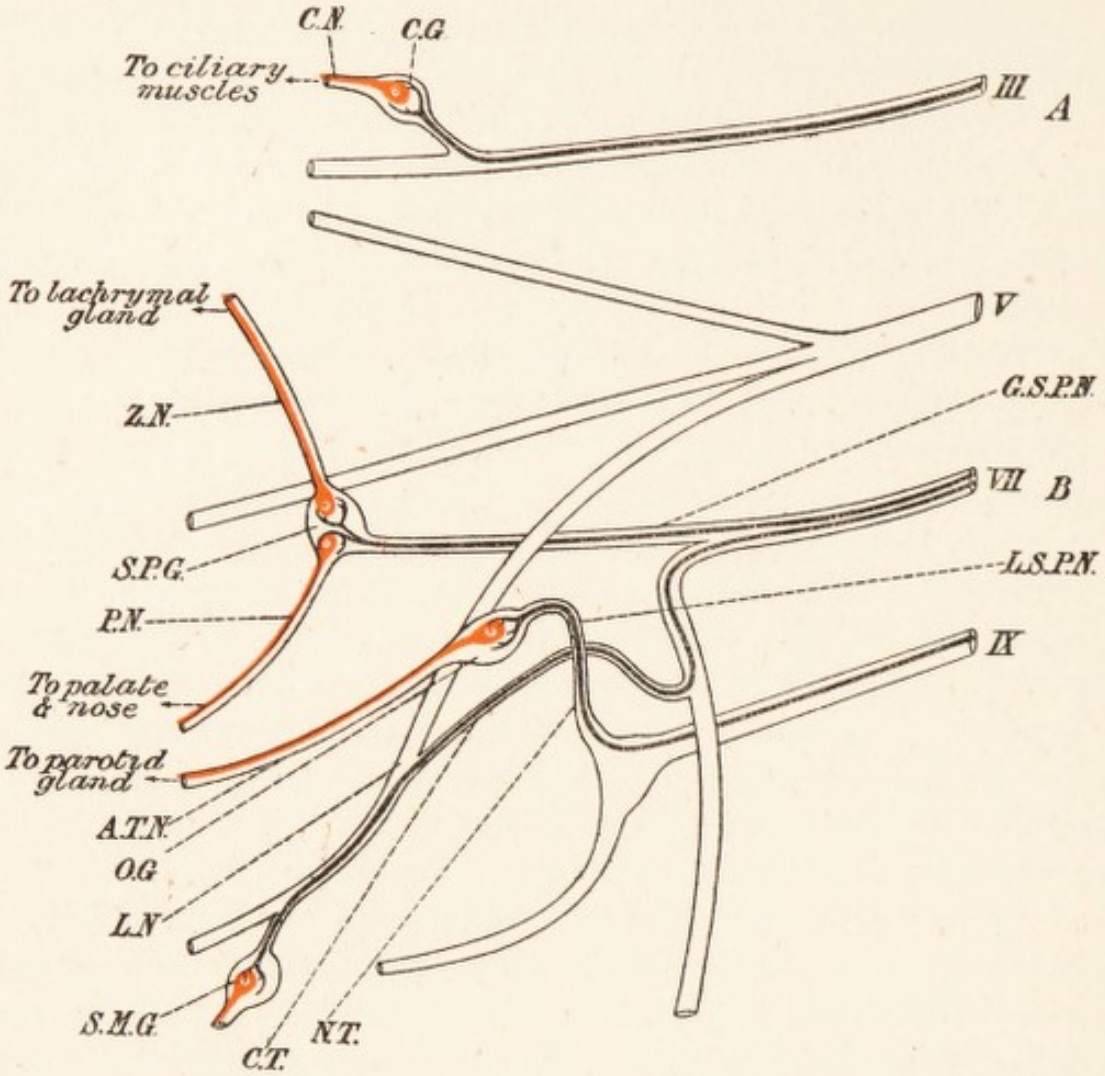


FIG. 6.—THE CONNECTOR FIBRES (BLACK) AND EXCITOR NEURONS (RED) OF THE INVOLUNTARY SYSTEM IN THE UPPER CRANIAL REGIONS.

A. The prosomatic group.

B. The upper part of the mesosomatic group.

A. The prosomatic group consists of connector fibres running in the third nerve to the ciliary ganglion, *C.G.*, in which lie the excitor neurons whose processes run in the short ciliary nerves, *C.N.*, to the ciliary muscles of the eye.

B. Three groups of connector fibres exist.

1. A group of connector fibres running in the seventh nerve to the spheno-palatine ganglion, *S.P.G.*, by way of the great superficial petrosal nerve, *G.S.P.N.* These connect with excitor neurons in the spheno-palatine ganglion, one group of which run in the zygomatic nerve, *Z.N.*, to the lachrymal gland, the other group of which run in the palatine nerves, *P.N.*, to the unstriped muscles and glands in the region of palate and nose.

2. A group of connector nerves which run in the seventh nerve, then pass into the chorda tympani, *C.T.*, and reach a submaxillary ganglion, *S.M.G.*, by way of the lingual nerve, *L.N.* The excitor neurons lie in the submaxillary ganglion and supply secretory fibres to the submaxillary gland.

3. A group of connector fibres which run in the ninth nerve and pass by way of the nervus tympanicus, *N.T.*, and the lesser superficial petrosal nerve, *L.S.P.N.*, to the otic ganglion, *O.G.* The excitor neurons in the otic ganglion run in the auriculo-temporal nerve, *A.T.N.*, to the parotid gland.

on the same plan as the voluntary nervous system, with receptor, connector, and excitor elements.

The marked difference is that the excitor elements have left the central nervous system and become peripheral, forming the various ganglia found throughout the body; while the receptor elements have remained in the same position as those of the voluntary system, namely in the posterior root ganglia, and connect by means of sensory root fibres with the cells of the connector elements, which have remained in the central nervous system; the connector fibres have passed out to reach their respective peripherally situated excitor elements. This outflow of connector fibres does not occur, at all events in the higher vertebrates, in every segment, but is interrupted at the places where the nerve plexuses for the upper and lower limbs come in; so that we can speak of three outflows of these fibres, a bulbar, a thoracico-lumbar, and a sacral. Of these the thoracico-lumbar outflow of connector nerves connect with all the excitor neurons of the so-called sympathetic system, the sacral outflow connects with another set of excitor neurons forming the pelvic ganglionic group, and the bulbar outflow connects with the excitor neurons found in the course of the various mesomatic segmental nerves.

In addition to these three main groups of connector nerves a fourth group exists confined to the region of the mid-brain, which connects with the excitor neurons forming the ciliary ganglion.

These connector fibres of the involuntary system leave the cord in the spinal region by the anterior roots, so that strictly speaking the anterior root is made up not of motor fibres, but of motor fibres to the voluntary system and connector fibres to the involuntary system; therefore as we do not think of speaking of the fibres of the pyramidal tract as motor fibres of the voluntary muscles, or as pre-ganglionic fibres, so also we ought not to speak of the corresponding fibres of the involuntary system as motor or pre-ganglionic but as connector fibres.

When I speak of the motor neurons of the involuntary nervous system as having travelled out from the central nervous system in separate outflows, I do not in the least intend to imply that in my opinion they have wandered out to their destination in the shape of free cells, but simply that their ultimate position has

become removed to a greater or less extent from their original position during the process of development.*

The next step in the investigation was obviously to find out the functions of these three outflows and so attempt to discover their meaning. It so happened, however, that my anatomical investigations had led me direct to the consideration of the segmentation of the vertebrate and the meaning of its central nervous system, a matter of such absorbing interest to me that I determined to continue to research on those lines; accordingly I asked Dr. (now Sir John) Rose Bradford to undertake the systematic investigation of the functions of the nerves in all the roots which contribute to these three outflows. He was very pleased to undertake the research and published as its first fruits the distribution of the vascular nerves in the thoracico-lumbar outflow.

A more extensive investigation of the functions of these roots was subsequently carried out by Langley and Anderson.

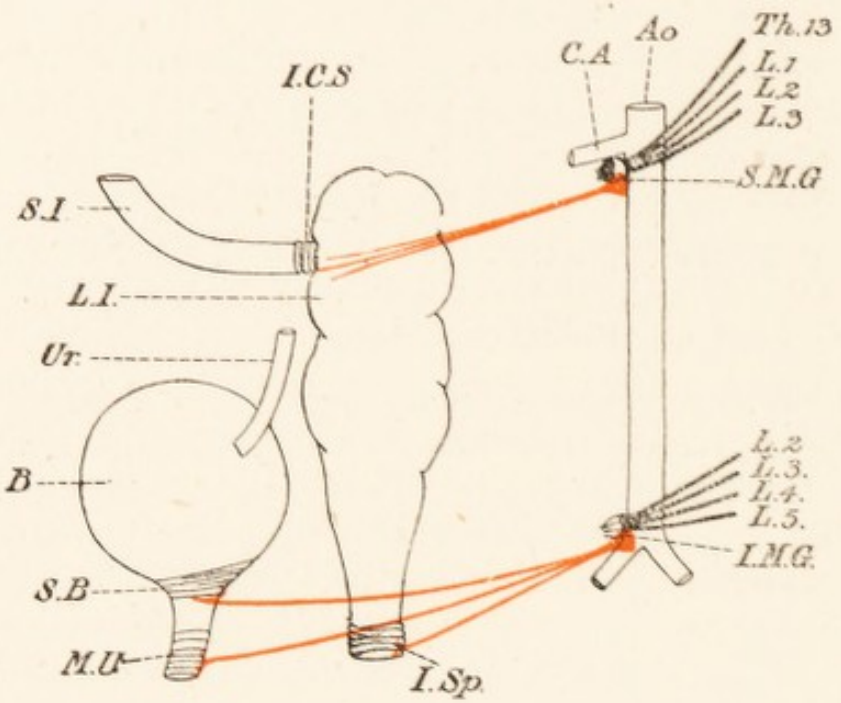
* In my opinion a sympathetic motor nerve cell has from the beginning always been in continuity with its particular peripheral organ (see Chap. XI).

CHAPTER II

THE CHARACTERISTIC MOTOR FUNCTIONS OF THE NERVE CELLS BELONGING TO THE THORACICO-LUMBAR OUTFLOW OF CONNECTOR NERVES; USUALLY CALLED THE SYMPATHETIC NERVE CELLS

I COME now to the question of the functions of the motor neurons belonging to the three outflows—cranial, thoracico-lumbar, and sacral. Have they all similar functions or are they clearly differentiated from each other? I propose in the first instance to confine myself entirely to the consideration of those cells which supply motor nerves to the various kinds of involuntary muscle, and to leave entirely to a later discussion the question of nerve cells which supply inhibitory nerve fibres to muscular structures, or fibres causing secretion of glands. In the present chapter I will consider in the first place the motor neurons connected with the thoracico-lumbar connector nerves (Fig. 4). The result is very instructive, for the evidence shows that: (1) the motor nerves for the muscles of the blood vessels over the whole body belong to this system; (2) the motor nerves for the musculature of the sweat glands over the whole body belong to this system; (3) the motor nerves for all unstriped muscle under the skin, whether pilo-motor or not, belong to this system; (4) the motor nerves for all unstriped muscle in connexion with structures derived from the segmental duct belong to this system (Fig. 8). In other words, the essential function of the neurons of the sympathetic system, so far as motor nerves are concerned, is to supply such nerves to a layer of unstriped muscle under the skin, around the blood vessels and around the tubular structures derived from the segmental duct. A further system also exists, namely (5) the motor nerves to the sphincters of the intestine (Fig. 7), but I will defer consideration of this system to the end of this chapter. I will now consider the first four groups one by one.

1. *The motor nerves to the blood vessels and to the heart.*—Two


I.C.S
C.A
Ao
Th.13
L.1
L.2
L.3
S.M.G
S.I
L.I.
Ur.
B
L.2
L.3.
L.4.
L.5.
I.M.G.
S.B
M.U
I.Sp.

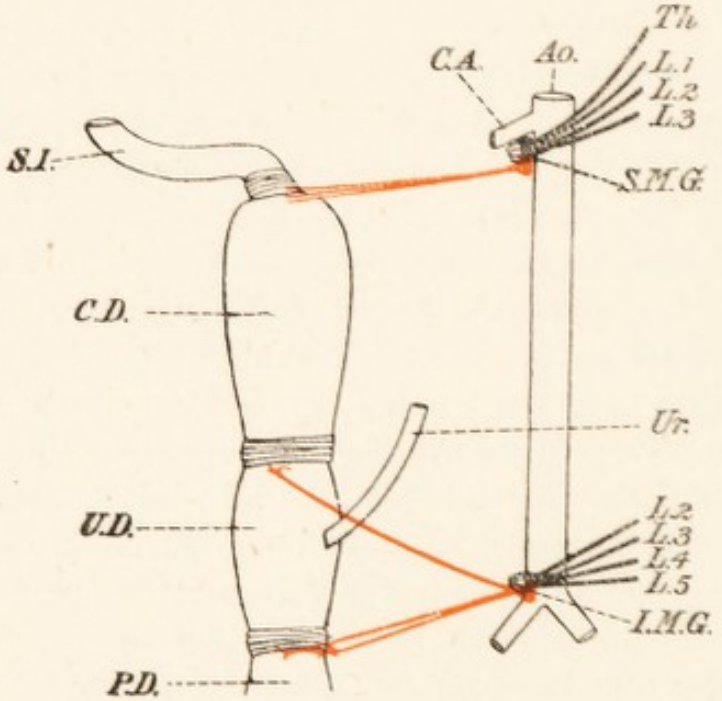

Th
C.A.
Ao.
L.1
L.2
L.3
S.M.G.
S.I.
C.D.
Ur.
U.D.
L.2
L.3
L.4
L.5
I.M.G.
P.D.

FIG. 7.—THE CONNECTOR FIBRES AND EXCITOR NEURONS OF THE SPHINCTER SYSTEM OF INVOLUNTARY MUSCLES.

The upper figure shows their arrangement in the mammal and the lower figure their arrangement in the reptile (young crocodile).

The connector neurons form two groups : an upper group rising from the last dorsal and first three lumbar roots and all running to the superior mesenteric ganglion, *S.M.G.*, which lies at the point of origin of the cœliac axis, *C.A.*, from the aorta, *Ao.*, and a lower group rising from the second to fifth lumbar roots, *L.*2 to *L.*5, and running to the inferior mesenteric ganglion, *I.M.G.*, which is situated just above the bifurcation of the aorta.

The excitor neurons from the superior mesenteric ganglion innervate the ileocolic sphincter muscle, *I.C.S.*, which lies at the junction of the small intestine, *S.I.*, and the large intestine, *L.I.*

The excitor neurons in the inferior mesenteric ganglion supply in the mammal the internal sphincter muscle, *I.Sp.*, the sphincter of the bladder, *S.B.*, and the muscle of the urethra, *M.U.*

The cavities of the bladder and large intestine are here entirely separate but have been evolved from the arrangement shown in the lower figure. In the reptile the cloaca is composed of a continuous tube divided into three portions. 1. The coprodœum, *C.D.*, which corresponds to the large intestine of the mammal. 2. The urodœum, *U.D.*, which corresponds to the bladder cavity of the mammal and into which the ureters, *Ur.*, open, and 3. the proctodœum, *P.D.*, which is the hindmost chamber. A muscle corresponding to the internal sphincter of the mammal separates the coprodœum from the urodœum, and is innervated by excitor neurons in the inferior mesenteric ganglion. A similar muscle also separates the urodœum from the proctodœum ; this corresponds with the sphincter muscle of the bladder and the muscles of the urethra, and is innervated by excitor neurons in the inferior mesenteric ganglion.

nerves of opposite function supply the heart, viz. the vagus, which inhibits its action, and the accelerator, which increases its action. Of these two it is generally recognized that the latter corresponds to the motor nerves of the blood vessels. The accelerator nerves were traced in warm-blooded animals in Ludwig's laboratory in 1871 by Schmiedeberg, and were found to proceed to the heart directly from the following sympathetic ganglia: the stellate ganglia, the ganglia on the annulus of Vieussens, and the inferior cervical ganglia. They arise from cells in these ganglia, which were subsequently found to be connected with the central nervous system by connector nerves, which leave the cord in the anterior roots of the upper thoracic nerves and belong therefore to the thoracic outflow (Fig. 4). On the other hand it was asserted for a long time that in cold-blooded animals the vagus nerve was an accelerator as well as an inhibitor nerve, that therefore there was no uniformity in this respect. Feeling sure that this was a mistake I determined to investigate the conditions in an animal, which was cold-blooded, but also to a slight extent warm-blooded; for this purpose I obtained some live crocodiles and found in them that the accelerator went to the heart from the ganglion stellatum and not from the vagus. I found also the same separation in the tortoise. I then carefully investigated the frog, and found an annulus of Vieussens and the accelerator fibres going off as in all other animals; but, because they passed to the heart with the vagus, stimulation of the latter nerve necessarily stimulated them too. There is therefore no exception; the motor cells, from which arise the motor nerves to the heart muscle, are connected with the thoracico-lumbar connector nerves in all cases.

With regard to the blood vessels, it has been argued that the hyperæmia of the lungs and cornea, which follows upon section of the vagus and intra-cranial trigeminal respectively, indicated the section of vaso-constrictor fibres in these two nerves; but, apart from the fact that there was no evidence of contraction of the blood vessels of these organs when the respective nerves were stimulated, it has been conclusively shown that the hyperæmia is the consequence of paralysis in the laryngeal region in the one case, and is due to the loss of sensation in the other. The only positive assertion of the motor innervation of an unstriated muscle, which may be looked upon as belonging to the vascular system outside the area of the

thoracico-lumbar outflow, is Roy's statement that the vagus is the motor nerve to the muscles in the spleen. That this is not so has been shown by Schäfer and Moore, who have given evidence for the origin of the motor fibres to the spleen from the thoracic region. They point out that Bulgak came to the conclusion that the fibres concerned with the innervation of the spleen pass to their distribution by way of the anterior roots from the third thoracic to the tenth thoracic and the greater splanchnic nerves of the left side only, thence through the semilunar ganglion by the nerves accompanying the branches of the splenic artery. They themselves find that the anterior roots concerned extend from the third thoracic to the end of the thoracico-lumbar outflow, and exist on both sides of the body, but the effect is more marked on the left side. By the use of nicotine intravenously injected they show that the splenic nerves continue to act, when stimulation of the cord produces no effect and stimulation of the splanchnic nerves produces only the very slightest appreciable contraction. The motor nerves to the splenic muscles therefore, like all other motor nerves to involuntary muscles, are not affected by nicotine ; consequently, if they existed in the splanchnics, they should show their action when the splanchnic is stimulated after a full dose of nicotine ; the hardly appreciable contraction which occurs may mean that a few motor nerves to the spleen exist in the splanchnic nerves, arising from some of the nerve cells of the lateral sympathetic chain, or that the contraction is due to adrenaline thrown out from chromaffine cells by the stimulation of the splanchnics (see p. 141). The conclusion is that the motor neurons for the splenic muscles are situated in the semi-lunar ganglion.

There is absolutely no evidence of any vaso-constrictor nerves in any of the other cranial nerves or in connexion with the sacral outflow. In all cases, wherever the blood vessels may be, their motor innervation comes from cells connected with the thoracico-lumbar outflow of connector fibres.

The systematic investigation of the anterior roots of this region by various observers, especially by Bradford and by Langley enables us to draw up the following table, showing the motor nerves to the blood vessels in an animal with seven lumbar vertebræ.

Situation of Blood Vessels.	Situation of Motor Ganglion Cells.	Roots Containing Connector Nerves.
Head and Neck.	Superior cervical ganglion.	1, 2, 3, 4, 5, thoracic; 2, 3, 4, give maximum effect.
Heart.	Ganglion stellatum and inferior cervical ganglion.	1, 2, 3, 4, 5, thoracic; 2, 3, give maximum.
Anterior extremity.	Ganglion stellatum.	4, 5, 6, 7, 8, 9, thoracic and 10 slightly.
Posterior extremity.	6th lumbar, 7th lumbar, and 1st sacral ganglion.	11, 12, 13, thoracic; 1, 2, lumbar and 3, lumbar slightly.
Kidney.	Renal ganglion.	4, 5, 6, 7, 8, 9, 10, 11, 12, 13, thoracic; 1, 2, 3, 4, lumbar.
Spleen.	Semilunar ganglion.	3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, thoracic; 1, 2, 3, lumbar.
Abdominal viscera.	Superior mesenteric ganglion and semilunar gang.	6, 7, 8, 9, 10, 11, 12, 13, thoracic; 1, 2, lumbar.
Pelvic viscera.	Inferior mesenteric ganglion.	1, 2, 3, 4, lumbar.

An examination of this table brings out the striking fact that the innervation of the blood vessels of the upper and lower extremities is practically continuous from one end of the thoracico-lumbar outflow to the other. Also the motor neurons for the blood vessels are situated both in the lateral and collateral chain of ganglia, the former being entirely devoted to the supply of motor nerves to the blood vessels belonging to the structures innervated by the segmental nerves, both spinal and cranial, including the central nervous system itself, as well as to the thoracic viscera, while the latter supply with motor nerves all the blood vessels of the abdominal and pelvic viscera.

In certain regions the motor nerves of the blood vessels have not been conclusively determined; e.g. the vessels of the brain, of the lungs and the coronary vessels of the heart. In all these cases the presence of vaso-constrictor nerves has been denied, or at all events clear evidence of their existence is wanting. Undoubtedly these vessels have muscular walls and equally undoubtedly nerve fibres can be seen in them. I for one cannot believe that muscles exist without motor nerves. The whole discussion is so bound up with the action of adrenaline that it is better not to discuss it here, but to leave it until I come to the action of adrenaline in its bearing upon the nature of the involuntary nervous system.

2. *The motor nerves to the sweat glands.*—Abundant evidence has been given that the secretion of sweat can be brought about by the stimulation of nerves, and it has been shown conclusively,

(1) that these nerves belong to the sympathetic system, and (2) that their connector fibres are in anterior roots.

Strictly speaking, the nerves which cause secretion of sweat ought to be left until I come to discuss the glandular nerves; they must, however, be introduced in this place as well, because the secretion of sweat is partly due to the contraction of a layer of unstriped muscle fibres, which surround the sweat glands and by their contraction squeeze the sweat out of the gland. The action of these muscles must be included when secretion of sweat is caused by the stimulation of a nerve. The evidence given by various observers, especially Langley, shows clearly that the connector fibres to the motor neurons supplying the sweat glands in the feet of both dog and cat invariably leave the spinal cord in the thoracico-lumbar outflow. Cases of section of the cervical sympathetic nerve in the human being show also that the same is true for the motor neurons supplying the sweat glands in the face and forehead.

ORIGIN OF THE NERVES WHICH ARE MOTOR TO THE MUSCLES OF THE SWEAT GLANDS IN THE CAT.

Situation of Glands.	Situation of Motor Ganglion Cells.	Roots Containing Connector Fibres to these Cells.
Fore foot	Ganglion Stellatum	4, 5, 6, 7, 8, 9, 10, Thoracic. Max. 6, 7, 8
Hind foot	6, 7, Lumbar 1, 2, Sacral	12, 13, Thoracic, 1, 2, 3, Lumbar. Max. 1, 2, 3

3. *The pilo-motor and skin motor nerves.*—In a paper published by Schiff in 1870 on the autonomy of the sympathetic, the author argued that the sympathetic nervous system was not an independent system, but was a part of the cerebro-spinal system, and based his conclusions largely upon his discovery of the pilo-motor nervous system. He described the erection of hairs on the tail of the cat. This observation of Schiff remained isolated and indeed forgotten, until Sherrington noticed the same phenomenon in the monkey, and conjointly with Langley pointed out the nature of the phenomenon in the monkey and cat.

Since this paper, Langley has worked out the details of this innervation very fully, and has also shown that the same laws apply to the erection of the feathers in birds, and to the movement of the spines of the hedgehog. The main results of his

observations have already been summarized in the previous chapter, the important points being the proof of the segmental nature of the terminal motor neurons of this group of involuntary muscles, which lie in the ganglia of the main sympathetic chain, and the non-segmental nature of the connector fibres connecting these neurons with the central nervous system. As the connector fibres to the whole of the ganglia of the main sympathetic chain leave the cord in the thoracico-lumbar outflow, it matters not whether the erection of hairs takes place on the head, body, or tail ; in all cases the motor neurons of the pilo-motor muscles connect with the central nervous system only in the thoracico-lumbar region.

The extent of the skin area, which is supplied by the connector fibres in any anterior root of the spinal nerves, is given in Langley's table, which I here reproduce.

CONNEXION OF THE SPINAL NERVES OF THE CAT FROM THE FOURTH THORACIC TO THE THIRD LUMBAR WITH THOSE LATERAL GANGLIA OF THE SYMPATHETIC INCLUDED BETWEEN THE GANGLION STELLATUM AND THE COCCYGEAL GANGLIA.

Spinal Nerve.		Sympathetic Ganglia.
Thoracic	IV	g. st.
	V	,,
	VI	,,
	VII	,, 4 5 6 7 8 9 Thoracic
	VIII	,, 4 5 6 7 8 9 10
	IX	,, 4 5 6 7 8 9 10 11
	X	– – – – 8 9 10 11 12 13
	XI	– – – – – – – – – 12 13 1 2 3 Lumbar
	XII	– – – – – – – – – – 13 1 2 3 4 5 6 7
	XIII	– – – – – – – – – – – 1 2 3 4 5 6 7 1 Sacral
Lumbar	I	– – – – – – – – – – – 2 3 4 5 6 7 1 2
	II	– – – – – – – – – – – – 3 4 5 6 7 1 2 3
	III	– – – – – – – – – – – – – 4 5 6 7 1 2 3 coc.

In close connexion with these muscles, which move hairs, are the unstriped muscles which move the skin, the contraction of which in hairless animals like man causes the appearance known as goose skin, also the unstriped muscles underlying the skin round the orifices of the body, such as the anus and vagina, such a muscle as the retractor penis, and the unstriped muscles in connexion with the movements of the globe of the eye and of the nictitating membrane.

In all cases the connector nerves to the motor neurons of this skin musculature come out in this thoracico-lumbar outflow,

and the motor nerves are necessarily distributed with the skin branches of the spinal nerve corresponding to the particular sympathetic ganglion. It may therefore be stated that, in addition to the motor neurons of the vascular system already considered, the ganglia of the main sympathetic chain consist essentially of segmentally arranged motor neurons to a system of involuntary muscles underlying the skin. I will call this system of unstriped muscles under the skin, the *dermal* system of involuntary muscles; and therefore conclude from the previous statements that the dermal system of involuntary muscles is exclusively supplied with motor fibres from cells in the vertebral or main chain of sympathetic ganglia (Fig. 4).

4. *The motor nerves of muscles surrounding the segmental duct.*—So far, except incidentally, I have not touched upon the great system of the splanchnic nerves, nerves which constitute the connector nerves to the collateral ganglia—the superior and inferior mesenteric ganglia, etc. The collateral ganglia have nothing to do with the segmental nerves, but are concerned entirely with the internal visceral organs situated in the abdomen and pelvis. In every case the motor cells to the blood vessels of any organ are found in the ganglion which supplies the organ itself with sympathetic nerves. Thus the semilunar ganglion supplies the stomach, liver, and spleen with sympathetic nerves and also the vaso-motor fibres to these organs; the superior mesenteric ganglion bears the same relation to the small intestine, and the inferior mesenteric to the large, with respect to all sympathetic fibres including the vaso-motor ones; the renal ganglion supplies similar fibres to the kidney, and the spermatic or ovarian ganglion to the blood vessels of the testis or ovary respectively.

We have however not exhausted the nerve cells belonging to the sympathetic system by the consideration of the lateral and collateral ganglia, for some of the medullated fibres of the lumbar splanchnic nerves travel still farther afield before they arrive at their appropriate nerve cells. These cells, which are motor cells, are situated mainly if not entirely close on to the muscles to which they supply motor nerves. This most important musculature, which is exclusively supplied with motor nerves from motor cells connected with the thoracico-lumbar outflow, constitutes a morphological system differing somewhat from the vascular and dermal systems already considered, for it consists of

all the muscles surrounding the Wolffian and Müllerian ducts, and since these ducts arise from the segmental duct, it may be called the segmental duct system of involuntary muscles (Fig. 8).

Before giving the evidence in support of this assertion I will first recall to the mind of my reader the embryological evidence of the meaning and fate of the segmental duct, so that the nature of the musculature in question may be clearly understood.

The primitive organs of excretion were the pronephric organs, which excreted into the cloaca by a single duct on each side known as the segmental duct. Later on, in the fishes and amphibia, another set of segmental tubules was formed, in close relationship with the generative organs, which excreted also into the segmental duct and so into the cloaca. These were the mesonephric organs or Wolffian body, as they are called. The neighbouring generative organs also come to make use of the segmental duct, and the original duct becomes split into two ducts, the one the Müllerian, conveying the genital products, the other the Wolffian, conveying the excretory products. Later on still, in reptiles, birds and mammals, more kidney tubules are formed in segments posterior to the mesonephric, known by the name of the metanephric tubules, and these form the permanent kidney. The Wolffian body now takes no part in urinary excretion, only the generative gland remaining, whose duct is the Müllerian duct.

The formation of the duct of the permanent kidney is thus described by Keith. "It arises as a bud from the dorsal side of the Wolffian duct, near the termination of that duct in the cloaca. At first it is a stalked bud with a narrow lumen; it rapidly extends forwards to the lumbar region behind the Wolffian body and behind the peritoneum. The stalk of the bud forms the ureter. The connexion of the stalk with the Wolffian duct is lost; the termination of the ureter migrates along the duct till it reaches that part of the cloaca which afterwards forms the bladder."

The Müllerian ducts become the Fallopian tubes and by their fusion the uterus is formed. The terminal part of the Wolffian ducts in the female disappear: in cases where they persist they are known as the ducts of Gärtner. In the male, the vas deferens and ejaculatory duct are formed from the Wolffian duct, and enter into the urogenital sinus at the place where the sinus

pocularis or uterus masculinus (the remnant of the Müllerian duct) opens into the urogenital sinus in the prostate gland.

Further, in the original cloaca the bladder and rectum formed

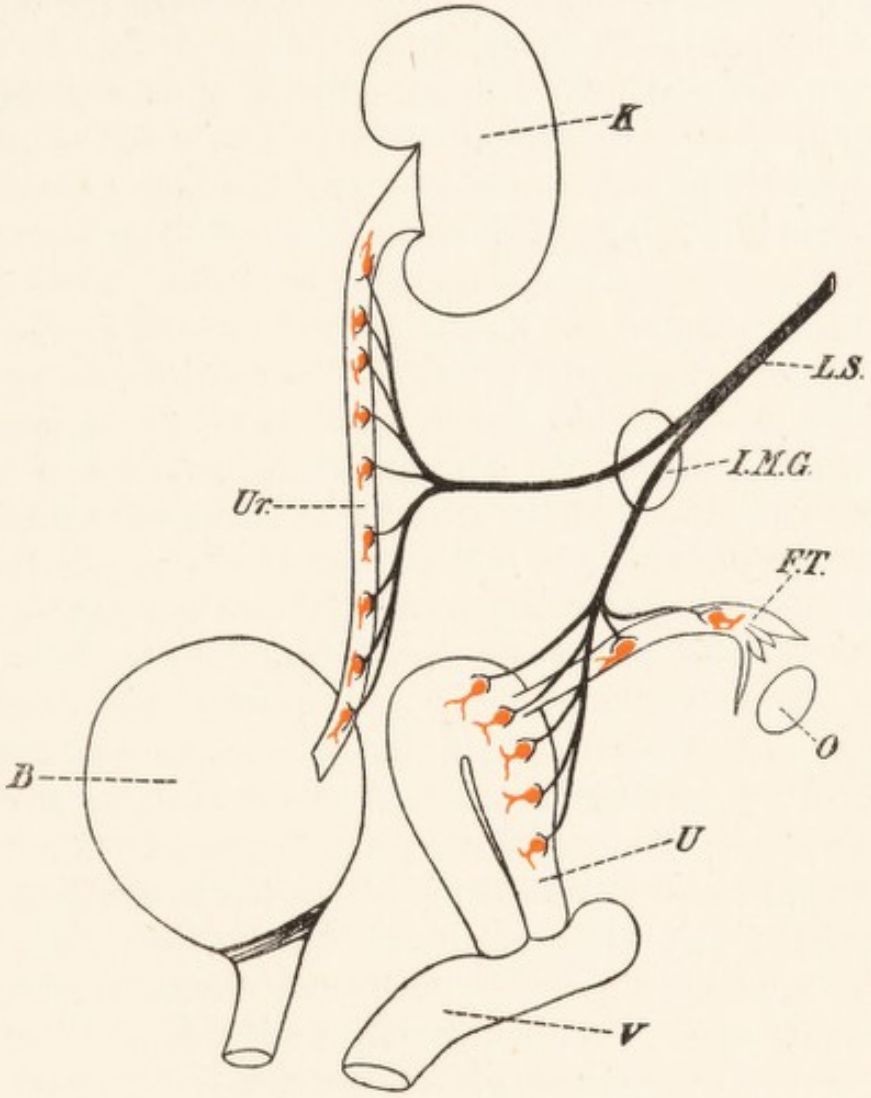


FIG. 8.—THE CONNECTOR FIBRES AND EXCITOR NEURONS OF THE UROGENITO-DERMAL SYSTEM OF THE FEMALE, THAT IS TO SAY THE SYSTEM SUPPLYING THE SEGMENTAL DUCT MUSCLES.

The connector fibres run in the lumbar splanchnic nerve, *L.S.*, and all pass through the inferior mesenteric ganglion, *I.M.G.* One set then runs to connect with motor neurons lying on the ureter, *Ur.* Another set connects with motor neurons lying on the uterus, *U.*, and the Fallopian tube, *F.T.*

O. Ovary.
V. Vagina.
B. Bladder.
K. Kidney.

a single cavity. In the course of growth the urogenital parts have separated entirely from the rectum and the bladder part of the cloaca and the rectal part open to the exterior by different openings. All these tubes are surrounded by unstriped muscle

both circular and longitudinal. This musculature is clearly derived from two sources, (1) the musculature surrounding the Wolffian and Müllerian ducts, i.e. the muscles of the ureters, uterus, and vas deferens; (2) the musculature of the cloaca, i.e. bladder, rectum, and large intestine.

The prostate gland, which is composed of tubular glands developed round the urogenital sinus, is largely surrounded with muscle which belongs partly to that surrounding the terminal parts of the Wolffian and Müllerian ducts (cp. Keith, *loc. cit.* p. 126, Fig. 101), and partly to the cloacal musculature.

Eckhard pointed out that stimulation of the nervus erigens caused a secretion of the prostate gland, which was not in his opinion a true secretion, but was caused by the contraction of muscles round the gland. This has been confirmed by Mislawsky and Borman who have shown that the nerve, which causes secretion of the prostate, is the hypogastric and not the pelvic and that, if the secretory nerves are paralyzed by atropine, there is still a temporary secretion on stimulation of the hypogastric, due to muscular action. Barrington confirms absolutely the results of Mislawsky and Borman, and points out that the mucin secretion of Cowper's glands and Bertholini's glands is also controlled by the hypogastric nerves; and that, as this effect of stimulation of the hypogastrics is abolished by the section and subsequent degeneration of the inferior splanchnics, it follows that the secretory nerve cells are not situated in the inferior mesenteric ganglia but peripherally at the glands themselves (Fig. 8). Therefore the fibres in the hypogastric nerves are not secretory fibres but connector fibres, which do not reach their secretory nerve cells until they arrive at the glands themselves. The same argument applies to the temporary secretion which is caused by contraction of muscles when the hypogastric nerve is stimulated. I conclude that the musculature around the prostate gland is partly cloacal and partly derived from the musculature of the uterus masculinus and of the ejaculatory duct.

The musculature of all these organs consists of two sets, longitudinal and circular; and v. Basch and Fellner, with other workers at Vienna, considered that the law of innervation throughout was a reciprocal innervation of these two sets of muscles by the pelvic nerve and the lumbar splanchnic respectively, the one being motor to the longitudinal muscles and in-

hibitory to the circular and *vice versa*. This law does not hold good for the uterus or the ureters or the vas deferens, for it has been shown conclusively that both motor and inhibitory fibres for the musculature of all these organs arise from nerve cells belonging to the lumbar outflow, there being no evidence that they are connected in the slightest degree with the pelvic nerve. The nerve cells with which they are connected form small groups on the course of the hypogastric nerves either near or in the organs themselves, as is seen in the isolated ganglia near the uterus and in the ganglia along the ureters, as Protopopow has shown.

The observations of Langley and Anderson prove clearly that all the motor neurons to the musculature surrounding the Wolffian and Müllerian ducts are connected with the central nervous system exclusively by connector nerves in the thoracico-lumbar outflow (Fig. 8). Further, according to Keith, these ducts are epiblast formations, and indeed the segmental duct, from which they are both derived, is in the opinion of many morphologists derived from the epiblast and not from the mesoblast. If this is the case then this musculature belongs to the system of skin musculature and its innervation is yet another proof that the motor nerve cells belonging to the thoracico-lumbar outflow, i.e. the sympathetic nerve cells, are *par excellence* the nerve cells which supply motor fibres to a very extensive system of unstriped muscles always lying just under the skin. As this system of muscles is especially connected with the internal genital organs and urinary ducts, I will call it the *urogenito-dermal* system to distinguish it from the *dermal* system already considered.

5. *The motor nerves of the sphincter system of gut muscles.*— So far I have shown that the connector thoracico-lumbar nerves connect with the motor neurons of three distinct systems of involuntary muscles, the vascular, dermal, and urogenito-dermal systems. There is yet another system to be considered, whose motor cells belong to the sympathetic, and which forms a distinct portion of the musculature of the gut.

The intestinal part of the gut is divisible into two portions, the small intestine and the large intestine or cloacal region. The motor nerve supply to these two portions is very striking and suggestive, for, as will be discussed more fully in the next chapter, the motor cells and nerves for the small intestine are connected

with the central nervous system by way of the vagus nerve, while the corresponding cells and nerves for the cloacal region are connected with the central nervous system by way of the pelvic nerve (Fig. 5). The small intestine is usually described as separated from the large by a valve, the ileo-cœcal valve; but, as Elliott has shown, there is in reality no valve here but a strong sphincter muscle, the ileo-colic sphincter, which terminates the intestine proper.

The hind gut originally formed a tube composed of three chambers, to which Gadow gave the names Coprodœum, Urodœum, and Proctodœum. The coprodœum was separated from the urodœum by a sphincter, and the urodœum from the proctodœum by another sphincter; thus relaxation of the urinary sphincter allowed the urine collected in the urodœum alone to pass out, while relaxation of the internal sphincter of the rectum as well as of the ordinary sphincter allowed the fæces to pass out (Fig. 7). The coprodœum has in the higher vertebrates separated entirely from the urodœum and opens directly to the exterior, still retaining its sphincter muscle, the internal sphincter of the anus. The urodœum or bladder opens to the exterior by way of the urethra and still retains its original sphincter muscle in the shape of the urethral muscles and the unstriped sphincter muscle.

Thus there are the following sphincter muscles which terminate the different regions of the gut:—

1. The ileo-colic sphincter at the end of the small intestine.
2. The internal anal sphincter at the end of the coprodœum.
3. The internal vesical sphincter and the urethral muscles at the end of the urodœum.

The motor nerve supply to all these muscles is arranged on a uniform plan (Fig. 7). Thus Elliott has shown that the ileo-colic sphincter contracts upon stimulation of the superior splanchnic nerves, and that its motor nerve cells are situated in the superior mesenteric ganglion. Langley and Anderson have shown that the internal anal sphincter contracts on stimulation of the inferior splanchnics and its motor nerve cells are situated in the inferior mesenteric ganglion. Finally Elliott has shown that the internal vesical sphincter and the muscles of the urethra contract on stimulation of the inferior splanchnics, and their motor nerve cells are situated in the inferior mesenteric ganglion.

The motor fibres of these sphincter muscles thus arise from

nerve cells in the superior and inferior mesenteric ganglia respectively, and are connected with the central nervous system by connector fibres in the thoracico-lumbar outflow (Fig. 7).

There are also muscles of the nature of sphincters at the fore end of the alimentary canal in the so-called pyloric sphincter, separating the pyloric end of the stomach from the intestine, and the cardiac sphincter between the œsophagus and the cardiac end of the stomach. The innervation of this foremost part of the gut has not been so definitely made out as that of the hinder part; I will consider it later in connexion with the movements of the stomach and œsophagus.

In my opinion this sphincter system must receive an explanation in the past history of the vertebrate. In my book on the "Origin of Vertebrates" I have come to the conclusion that the vertebrates arose from the great group of the Appendiculata, i.e. arthropods and worms, and that the neural canal with its peculiar enlargements in the form of the ventricles was originally the alimentary canal of the invertebrate ancestor, the infundibulum being the original œsophagus. As the animal remained upright this necessitated the formation of a new alimentary canal on the ventral side of the body. The evidence is strongly in favour of the view that the essential factor in the formation of this new alimentary canal was a respiratory chamber, in which were included a series of respiratory appendages supplied by a group of segmental nerves, which afterwards became the vagus, glossopharyngeal and facial group of nerves. I have given reasons for the belief that such a respiratory chamber originally extended close up to the cloacal region of the animal and ultimately became connected with the cloaca by a tube. Originally in my opinion there was a short groove situated in the mid-ventral surface of the body between the respiratory chamber and the cloaca. Surrounding this mid-ventral groove, just as in the Trilobites and Apus, were situated a series of appendages not necessarily respiratory, but serially homologous with the respiratory appendages in the branchial chamber. This groove became converted into a tube which formed the original very short intestine, connecting the respiratory chamber with the cloaca. The muscles of an intestine so formed would be essentially those belonging to the non-respiratory appendages, and supplied therefore with motor fibres from cells connected with the vagus group

of nerves. In addition the ventral groove itself may have contributed some muscles underlying the ventral skin to the formation of this muscular tube.

With the subsequent elongation of this new-formed intestine, the respiratory chamber became farther and farther removed from the cloacal region, thus giving rise to the long intestine of the vertebrate, the muscles of which, supplied as they are by the vagus, demonstrate its origin from a prolongation of the respiratory chamber; while at the same time a muscular layer underlying the ventral skin, which, I suggest, helped to form the original short tube, would still remain and form the sphincter system of muscles whose motor nerve cells are situated in the mesenteric ganglia of the sympathetic.

The whole evidence points to the conclusion that the motor nerve cells, which are connected with the central nervous system by the thoracico-lumbar outflow of connector nerves, supply with motor fibres the whole of the vascular musculature and the whole of a system of unstriped muscles, which originally was lying just under the skin, and also formed the sphincter system in the gut: this latter system may have originated from the dermal musculature, but at present we have no direct evidence of such an origin. It conforms to the rest of the dermal musculature, not only in its innervation, but also in its behaviour to the action of adrenaline, thus showing that its characteristics are those of the dermal musculature and not of the neighbouring muscles of the gut. I would suggest therefore the inclusion of the sphincter muscular system under the general title of dermal musculature. Whether the vascular musculature is closely related to the dermal musculature morphologically I am not at present prepared to discuss; but the close relationship chemically between the two muscular systems is proved beyond doubt by the similar action of adrenaline.

In order to express in one term the whole of the group of muscles discussed in this chapter, the title "the sympathetic group of muscles" might be used, although it would be better to entirely abolish the meaningless term "sympathetic" from vertebrate anatomy. I would suggest as a temporary substitute for the term "sympathetic" the word "vaso-dermal" in describing this muscular group, meaning by the term all the vascular muscles and dermal unstriped muscles throughout the body.

We may then sum up the results of this chapter as follows: The motor cells of the so-called sympathetic system, which are connected with the central nervous system by the thoracico-lumbar outflow of connector nerves, form that part of the involuntary system which supply motor nerves to all the muscles of the vascular system and to a 'dermal' system of muscles originally lying under the skin. This dermal system is divisible into three groups:—

1. The *dermal or ectodermal system* proper, the motor cells of which are in all cases situated in the lateral sympathetic ganglia, and send motor fibres to all the involuntary muscles in the body, which are still lying just under the skin.

2. The *urogenito-dermal system*, the motor cells of which are in all cases situated in or near the muscles themselves and send motor fibres to all the involuntary muscles which originally surrounded the Wolffian and Müllerian tubes.

3. The *alimentary canal system*, the motor cells of which are in all cases situated in the mesenteric ganglia, and send motor fibres to sympathetic muscles which have helped to form the new gut, and still exist as sphincters in that gut.

There is thus, it seems to me, evidence of a marked unity in the sympathetic nervous system, which separates it from the other members of the involuntary system, and such unity is further shown by the extraordinary action of adrenaline. Oliver and Schäfer discovered that an extract of the suprarenal glands injected into the circulation caused a rise of blood pressure due to the contraction of the muscles of the blood vessels, and that the substance which caused this effect was contained in the medullary and not in the cortical portion of the gland. The substance in question was subsequently isolated by Takamine and has received the name of adrenaline, adrenine, or epinephrine. Its constitution is now known.

Since this discovery a large amount of work has been done on this subject especially by Lewandowsky, Langley, Elliott, Biedl, and others, which has firmly established the following conclusion. Adrenaline acts only on those tissues which are innervated by the sympathetic nervous system, and its action is always the same as that of the sympathetic nerves supplying the tissue. If their stimulation causes contraction then adrenaline causes contraction, if it produces inhibition, so does adrenaline.

The substance is absolutely ineffective on all tissues which are innervated by the nerve cells of the cranial or sacral outflows. In adrenaline then we possess an extraordinary means of checking the conclusions arrived at by stimulation of the nerves belonging to the thoracico-lumbar outflow. The selective action of adrenaline is not on the central nervous system, for it acts more powerfully on the denervated organ and even after all the nerves going to the organ have been allowed to degenerate.

This intimate relationship between the action of adrenaline and that of the sympathetic nervous system is most extraordinary and the reason for it will be considered later. It has naturally been utilized for the investigation of such doubtful cases as the existence of motor nerves to the blood vessels in the case of the arteries of the brain, of the lungs, and of the heart, in all of which the existence of vaso-constrictor nerves has been doubted. In all these cases the action of adrenaline has proved the existence of such nerves, even though their action is weak. Thus Biedl and Reiner have seen contraction of the blood vessels of the brain upon direct application of adrenaline, and Protopopow and Wiggers found there was a distinct diminution in the outflowing blood upon the addition of adrenaline to the fluid circulating through the brain. With respect to the lung vessels Brodie and Dixon could find no evidence of constriction by adrenaline, but Plumier and Wiggers found a distinct diminution in the rate of flow through the lungs when fluid containing adrenaline was sent through. Führer and Starling also obtained a distinct rise of pressure in the pulmonary artery, by adding adrenaline to the perfused blood in the heart lung preparation. Tribe also found that if the pressure in the pulmonary artery was not above the normal, adrenaline always caused a marked diminution of flow through the lung; and also obtained some evidence of vaso-constriction by direct stimulation of the stellate ganglion. In the case of the coronary vessels of the heart adrenaline is said to cause dilatation not constriction, but Brodie and Cullis think this is due to the strength of adrenaline used being too great. When they sent an artificial circulation through the rabbit's heart, to which a weak dose of adrenaline had been added, the first effect, which lasted as long as 80 seconds, was a diminution of flow through the coronary vessels followed by a marked increase of flow. This dilatation, which has often been observed, can be explained

by the experiments of Markwalder and Starling as being due to non-volatile metabolites produced by the heart muscle itself. Such experiments therefore all tend to show that the innervation of the vessels of these doubtful organs is the same as in all other cases.

CHAPTER III

THE CHARACTERISTIC MOTOR FUNCTIONS OF THE NERVE CELLS BELONGING TO THE BULBO-SACRAL OUTFLOW OF CONNECTOR NERVES

THE motor nerve cells, which supply motor fibres to involuntary muscles associated with the cranial nerves, fall into two distinct groups in accordance with the natural division of these nerves into a foremost or prosomatic and a hindmost or mesosomatic group. In each of these groups motor nerve cells to involuntary muscle are found situated outside the central nervous system, those in the ciliary ganglion belonging to the prosomatic region and those in connexion with the bulbar group of nerves to the mesomatic region. In this chapter I propose to deal with the latter group and to consider their functions at the same time as those of the motor nerve cells of the sacral outflow on account of the close functional relationship of these two outflows.

In the sacral outflow there are undoubtedly motor nerve cells which are not situated in the central nervous system, but connect with it by means of the pelvic nerve. The position of the motor neurons and their connexion with the central nervous system by means of the vagus and pelvic nerves respectively resemble so closely the arrangement of the sympathetic motor neurons, as to make it almost certain that these communicating fibres in the vagus and pelvic nerves must both be regarded as connector fibres to motor neurons. The embryological evidence that the latter have travelled out from the central nervous system to the periphery has already been mentioned in Chapter I. and will be given more fully in Chapter VIII.

In all mammals without exception contraction of the unstriped muscles of the small intestine takes place upon stimulation of the vagus nerve, and Bayliss and Starling have proved, by means of the enterograph, that both longitudinal and circular muscles contract when the vagus is stimulated, and that neither contract

on stimulation of the splanchnic nerve. I have already discussed the share taken by the sympathetic system in the innervation of the small intestine but have not considered the stomach and œsophagus. As far as concerns the œsophagus and its termination in the cardiac sphincter of the stomach, there is no evidence that sympathetic motor fibres reach to this region; the motor supply is entirely from motor cells connected with the vagus nerve. The passage of food from the stomach to the intestine is regulated by a sphincter muscle at the pylorus, and there is some evidence to show that a musculature exists here which is innervated after the same fashion as the rest of the sphincter group of muscles already considered. Elliott has given evidence of some contraction of this sphincter muscle in the rabbit upon stimulation of the splanchnic nerve, and he finds in the bird a contraction of the whole of the duodenal region upon stimulation of the same nerve. Still more extensive is this musculature in the frog, according to the evidence of Dixon, who states that the musculature of the whole stomach of that animal contracts either upon stimulation of the splanchnic or in consequence of the direct action of adrenaline. There are then indications in this region of a musculature supplied with sympathetic motor fibres which varies in its extent in different animals, just as according to Elliott (see p. 57) the corresponding sphincter musculature of the bladder varies greatly. Undoubtedly, as in the small intestine, the musculature of the main body of the stomach in all mammalia is supplied with motor fibres from cells connected with the vagus nerve.

Where then are the motor cells to this intestinal unstriped musculature, to which the vagus fibres are the connector nerves? In such a very low vertebrate as the lamprey the fibres of the vagus nerve can be traced in the walls of the intestine and, scattered along the nerve fibres, nerve cells can be seen with which they are in connexion. These scattered nerve cells include among them the motor cells to the intestinal muscle and are situated in the walls of the intestine itself. In the higher forms of vertebrates these nerve cells form a characteristic layer between the circular and longitudinal muscles of the intestine and, with the nerve fibres in connexion with them, are known by the name of Auerbach's plexus. The cells of Auerbach's plexus must in my opinion be regarded as the motor nerve cells, from

which arise motor nerves to that part of the involuntary intestinal musculature, which is associated with the vagus portion of the cranial outflow of connector nerves; just as some of the motor cells in the mesenteric ganglia give origin to motor fibres to that part of the involuntary intestinal musculature, which is associated with the thoracico-lumbar outflow, namely, the sphincter system (Fig. 5).

In the region of the œsophagus such motor cells are still found, but no longer in the same position as in the intestine: they have come more to the surface so that they form a superficial plexus lying on the unstriped muscle of the œsophagus.

A diverticulum of the intestine forms the lungs, and this diverticulum carries with it the same innervation as the intestine from which it was derived; its voluntary musculature, as in the pharynx and œsophagus, receives motor fibres direct from the motor cells of the *nucleus ambiguus* in the medulla oblongata; its involuntary musculature, the unstriped muscles surrounding the bronchi, receives motor fibres from motor cells in the lungs themselves, and the vagus nerve supplies connector fibres to these nerve cells (Fig. 3, B and C).

Another diverticulum of the intestine forms the liver, the gall bladder of which is surrounded by unstriped muscles. The motor cells which supply motor fibres to this musculature are, according to Bainbridge and Dale, situated in the organ itself and their connector fibres belong to the vagus nerve.

The part of the intestine associated with the vagus nerve finds its lower limit at the end of the small intestine. The vagus never sends fibres into any part of the large intestine. The large intestine is however part and parcel of the tube of the alimentary canal, and one would naturally expect it to be innervated in the same manner as the small intestine, although its motor cells are connected with the central nervous system by connector fibres in the pelvic nerve arising from the sacral end of the body, while those of the small intestine are connected with the central nervous system by connector fibres in the vagus nerve arising from the cranial end of the body.

I will now consider the sacral outflow and determine what is the great characteristic of the motor nerve cells belonging to this group. Their connector fibres pass, as already mentioned, from the spinal cord in the anterior roots of the 2nd and 3rd sacral

nerves and form a single nerve (the pelvic nerve) on each side, which passes direct to the bladder without dipping down into the pelvis to join the lateral chain of ganglia (Fig. 5).

The groups of cells on the bladder and rectum, with which this pelvic nerve communicates, have received the title of hypogastric plexus, which is misleading, as these cells have very little to do with the hypogastric nerve and are chiefly concerned with the pelvic nerve ; it is better therefore to discard this term and to call this collection of nerve cells and nerve fibres the pelvic plexus, as Langley has done.

The great characteristic of the sacral outflow is that its motor nerve cells supply with motor nerves the cloacal region of the alimentary canal. In the cloacal region I include the large intestine and the bladder, for the origin of the bladder is from the cloaca. There is no evidence whatever that the pelvic nerve ever supplies any part of the small intestine, just as there is no evidence that the vagus nerve ever supplies any part of the cloacal region.

In the large intestine there are, as in the rest of the intestine, both circular and longitudinal muscles, and it has been taught, especially by the Vienna school, that the motor nerve supply from the sacral region was confined to the longitudinal muscles and that the circular muscles were supplied from the lumbar splanchnics, the inhibitory nerves arising respectively from the opposing region. Such a scheme of reciprocal innervation has been put forward for all hollow organs possessing longitudinal and circular muscles, and in no case has it been established. Certainly in the case under consideration it is not true. Bayliss and Starling by means of the enterograph especially studied this question, and proved that both sets of muscle contract when the pelvic nerve is stimulated. Langley and Anderson confirm this observation and find indeed that the whole of the large intestine receives its motor supply from the nerve cells belonging to the sacral outflow, with the exception of the internal sphincter ani which, as already mentioned, is supplied by cells belonging to the thoracico-lumbar outflow. Elliott has confirmed this by the injection of adrenaline, which causes no contraction whatever of any part of the large intestine with the exception of the internal sphincter ani.

The musculature of the bladder is the remaining portion of

the cloacal musculature which is supplied with motor nerves from nerve cells connected with the pelvic nerves. All observers, from the earliest times, are agreed that stimulation of this nerve causes a strong contraction of the bladder in all animals which possess one.

The sacral outflow differs from the thoracico-lumbar in a striking manner; whereas the latter passes into well-defined ganglia, which give origin to efferent fibres often having to travel to some distance before reaching their destination, the former pass directly, not into a single ganglion, but into a nerve plexus, throughout which scattered nerve cells or small groups of nerve cells are found, lying close to the muscle itself. This pelvic plexus extends over the surface of the bladder and rectum, so that it is possible to speak of it as made up of a vesical and rectal plexus. Fibres pass from it to supply the large intestine, bladder, and urogenital tract. Langley and Anderson have followed out the course of the fibres to a considerable extent into and through this plexus, and have determined the end stations of many of the connector fibres by means of the degeneration method. The pelvic nerve was cut, and time allowed for degeneration of its medullated fibres. The different branches were then teased out after staining with osmic acid, and the number of degenerated fibres counted in each nerve examined. The results are shown in an illustration which is reproduced on the opposite page (Fig. 9).

The pelvic nerve divides primarily into an anterior and posterior branch; the latter connects with the rectal plexus, from which arise nerves running directly into the intestinal wall; these nerves Langley and Anderson designate as sacral colonic nerves, in contradistinction to the lumbar colonic nerves arising from the inferior mesenteric ganglion. They have shown that these sacral colonic nerves pre-eminently cause contraction of the muscles of the large intestine, while the lumbar colonic nerves cause essentially inhibition.

The first ganglion, or rather group of ganglia, lying in the rectal plexus on this posterior branch of the pelvic nerve, is a fairly conspicuous one; and they speak of it as the ganglion concerned with the motor nerves to the large intestine. An examination of the analysis of these sacral colonic nerves, as given in Fig. 9, shows that the large majority of the medullated fibres of these nerves are degenerated after section of the pelvic nerve,

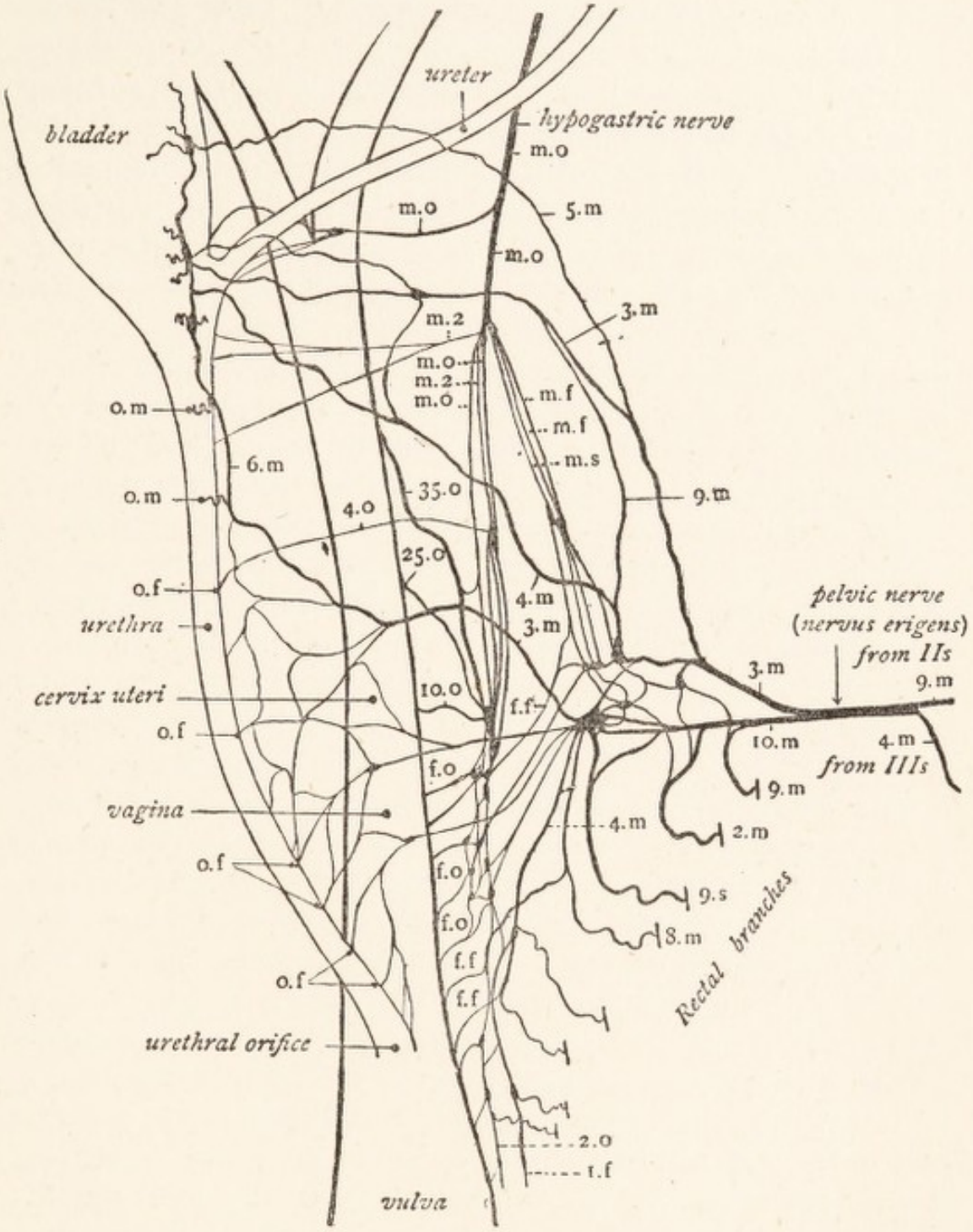


FIG. 9 (from Langley and Anderson, the "Journal of Physiology").

Left pelvic plexus of cat. The three sacral nerves and the first coccygeal nerve were cut peripherally of the spinal ganglia, and eleven days allowed for degeneration.

The numbers placed opposite each strand show the number of normal and of degenerated fibres present in it—the number of normal fibres being placed first. Thus 35·0 indicates that the strand contained thirty-five normal fibres and not one degenerated; m signifies many fibres (more than twenty-five); s signifies some (ten to twenty-five); and f, a few fibres (nine or less). Thus 9·m signifies that nine sound and more than twenty-five degenerated fibres were present in the strand.

only a few being left intact. The few normal fibres still left in the sacral colonic nerves must belong to the hypogastric nerve, a part of which also runs through the pelvic plexus, either being sensory fibres or possibly connector fibres to motor nerve cells belonging to some part of the internal sphincter of the anus. In another experiment, where both anterior and posterior roots of the cauda equina were cut between the posterior root ganglia and the cord, and time allowed for degeneration, so that the efferent fibres alone would degenerate, these sacral colonic nerves were found to possess a large amount of intact fibres. Langley and Anderson therefore come to the conclusion that the medullated fibres in these nerves are largely sensory, and that the motor cells for the large intestine are mainly situated in the part of the pelvic plexus which lies directly on the rectum and gives origin to the sacral colonic nerves. Similarly, the anterior branch of the pelvic nerve connects with the vesical plexus, in which lie the motor cells of the muscles of the bladder.

I conclude therefore that, for the main mass of bladder musculature and the musculature of the large intestine, the motor cells are situated, not in large isolated ganglia, but in a plexiform arrangement directly upon the surface of the musculature itself; an arrangement of the same kind as is found in the small intestine, where there exists a plexus with nerve cells, known by the name of Auerbach's plexus, the cells of which form the motor cells of that part of the gut, and are connected with the connector fibres of the vagus nerve (Fig. 5).

Further, if this pelvic plexus is the homologue of Auerbach's plexus, then instead of being between the circular and longitudinal layers it has come out upon the surface of the cloacal part of the gut, just as Auerbach's plexus lies on the surface of the unstriped muscle of the œsophagus at the other extremity of the gut, instead of between the circular and longitudinal muscular layers.

The comparative anatomy of the hinder part of the gut points to the coprodœum and urodœum as forming originally a continuous tube (Fig. 7). Consequently we should expect a similar innervation of the muscular layers of the two parts. In all probability some of the efferent fibres in the sacral colonic nerves are connector fibres to nerve cells situated more peripherally in the walls of the large intestine, and such cells would, if this is the

case, represent the portion of Auerbach's plexus in the large intestine itself. As already mentioned, the pelvic nerve has no connexion with any of the cells of the inferior mesenteric ganglion.

In addition to the contraction caused by stimulation of the motor supply to the bladder connected with the pelvic nerve, it has long been recognized that stimulation of the hypogastric nerve also causes some vesicular contraction, and consequently the bladder is supplied with motor fibres which arise from nerve cells belonging to the thoracico-lumbar as well as the sacral outflow.

Now it is a striking fact that the contraction of the bladder, seen when the hypogastric nerve is stimulated, does not in most cases involve the whole of the organ, but is confined to its neck and base; the part affected being roughly a triangular area, called the trigonum, whose apex is at its neck, and whose base is formed by a line joining the openings of the two ureters into the bladder.

According to Elliott, who has made a study of the nature of this contraction, it varies considerably in different animals, being confined to the base and neck in the dog, cat, monkey, rabbit, pig, and mongoose. In both the ferret, and Indian civet cat, the contraction on stimulation of the lumbar nerves extends over the whole bladder, but at the same time the sacral nerves cause also upon stimulation a full contraction of the whole organ. In the female goat the contraction caused by hypogastric stimulation is like that in the dog and cat, but in the male goat it resembles that in the ferret and extends over the whole organ. The bladder of the female goat is of larger volume than that of the male goat, which in its strong walls and small volume resembles that of the ferret. In all cases the results of nerve stimulation were confirmed by the action of adrenaline.

My own interpretation of these observations of Elliott is that, in such cases as the ferret and male goat, the musculature belonging to the sympathetic system has spread farther over the bladder than usual and has thus added another coat to the cloacal musculature, but the morphological differentiation of the two musculatures still exists, and is in all cases shown by the action of adrenaline. Elliott's objection to this view, that the bladder in the frog and toad is purely cloacal in origin, and yet its musculature is supplied with motor nerves from the 7th nerve root, which represents the lumbar outflow, as well as

the 9th and 10th nerve roots representing the sacral outflow, does not appear to me to be based on evidence so strong as to overthrow the evidence of other animals. It is true enough that we must attribute a double nerve supply to the frog's bladder corresponding to that of other animals, for adrenaline causes a contraction of the whole bladder, but this only makes one wonder whether it is right to describe the frog's bladder as purely cloacal. Although the two ductūs deferentes (ureters) open into the dorsal wall of the cloaca opposite the bladder orifice and not into the bladder, yet the bladder always contains pure urine unmixed with fæces. The mechanism by which this end is attained is thus described by Gaupp; by the action of sphincter muscles on the main cloacal tube above and below the orifice of the bladder, a urinary chamber is formed into which the ureters open and thus fill the bladder with pure urine; further, seeing that the urine is discharged from the bladder clear as water, it follows that normally the sphincter between the rectum and the bladder is kept closed, and the fæces are held back at the lower end of the rectum, which arrangement in fact functionally corresponds to the internal sphincter ani of the higher vertebrates. With such an arrangement it is perfectly possible that muscles belonging to the sympathetic system may have spread over the bladder and that the bladder musculature may not belong exclusively to the purely cloacal muscles. Again Kalischer has come to the conclusion that this trigonal musculature is different from the musculature of the main body of the bladder, "being characterized by the closeness of its constituent fibres and thus differentiated from the coarser muscular tissue of the bladder proper." It is on the contrary of the same kind as that of the urethra and ureters.

The morphological separateness of this vesicular sympathetic musculature from the vesicular cloacal musculature, is further shown by the phenomenon called by Langley and Anderson the "axon reflex." It was found by Sokownin that, when the inferior mesenteric ganglia were isolated from the central nervous system by the division of the nerve fibres on the abdominal aorta and of the lumbar splanchnic nerves on both sides, then, if the hypogastric on one side was cut and that end stimulated which is connected with the inferior mesenteric ganglion, contraction of the bladder was caused through the medium of the hypogastric nerve of the opposite side; as though the stimulation of the hypogastric

nerve brought about a contraction of the bladder reflexly through the isolated inferior mesenteric ganglion. Langley and Anderson investigated this apparent reflex and not only confirmed the fact, but showed also that the reflex was not confined to the bladder, for there occurred distinct pallor of the rectum and contraction of the internal sphincter muscle of the anus, when the cut hypogastric was stimulated. The part of the bladder involved was the trigonal area, and the reflex in all cases disappeared when nicotine was injected, showing that nerve cells were involved in the course of the reflex.

Further they showed that the effect of stimulation of the lumbar splanchnics was not confined to one side, proving that a stimulation of connector fibres could reach the opposite hypogastric nerve by way of the paired inferior mesenteric ganglia. Finally, by the method of degeneration, they showed that the hypogastric fibres, on which the reflex depended, had their nutritive cells in the central nervous system and that, therefore, when the lumbar splanchnics were cut on the one side and time allowed for their degeneration, the Sokownin reflex was no longer possible. The conclusion to which they came was that this reflex is not a true reflex in the ordinary sense of the word, but one brought about through the connector fibres of the lumbar splanchnics only ; the explanation being that a connector fibre in the lumbar splanchnic nerve passes along the hypogastrics to connect with a motor nerve cell of the internal sphincter ani muscle, which is situated near the muscle itself. This fibre gives off a collateral to connect with a nerve cell in the inferior mesenteric ganglion of the opposite side, which supplies motor fibres to the internal sphincter ani of that side. This collateral is excited because it is part and parcel of the same axis cylinder as that of the fibre stimulated. A similar argument applies in the case of the reflex on the trigonal part of the bladder and the muscles of the rectal blood vessels. They have never seen any such reflex on the uterus, or any of the internal genital organs, which would imply that no nerve cells supplying motor fibres to these muscles are situated in the inferior mesenteric ganglia, or if so, that there is no connexion between the two sides of the body.

In addition to this reflex Langley has found exactly similar phenomena in ganglia of the lateral chain.

These axon reflexes constitute one of the chief arguments in

favour of the view that the connector nerve fibres of the involuntary nervous system, which constitute the thoracico-lumbar outflow, behave like those of the voluntary nervous system, and give off collaterals to a number of ganglion cells; in consequence of such collaterals an axon reflex can take place in organs entirely separated from the central nervous system. Further there is no reason to suppose that one part of the involuntary nervous system differs in essentials from another. I imagine therefore that the cranial connector fibres in the vagus nerve and the sacral connector fibres in the pelvic nerve also send off collaterals, so as to connect with more than one motor nerve cell; that therefore, when the organs supplied by such motor cells are isolated from the central nervous system, reflexes can take place in them which are also of the nature of axon reflexes, and thus may account for the reflexes observed in the isolated heart, intestine, and bladder. This question will receive further consideration in a later chapter.

The sympathetic musculature, which becomes part of the bladder musculature, may have arisen from one or both of the two systems, which I have called the urogenito-dermal and the sphincter systems, by means of the involvement of the musculature of the ureters in the one case, and of the sphincter muscles of the bladder and urethra in the other. The physiological evidence is in favour of the vesical sphincter system as playing the chief part in the formation of the muscles in question, for the phenomenon of the axon reflex shows that the two marked reflex contractions, which take place through the medium of the mesenteric ganglia upon stimulation of the central end of the hypogastric nerve, are those of the trigonal region of the bladder and of the sphincter ani, and further that the motor fibres to the muscles in each case arise from cells in the inferior mesenteric ganglion. In other words, the vesicular musculature involved in this reflex is innervated in the same manner as the internal sphincter ani, and belongs to the sphincter muscular group and not to the urogenito-dermal.

As already stated, the axon reflex is brought about by the presence of collaterals in a connector fibre belonging to the lumbar splanchnic nerves, one of which connects with a motor cell in the inferior mesenteric ganglion and the other with a nerve cell near the muscle itself. This motor cell sends motor fibres

to the muscle and so causes its contraction. It is possible that the nerve cell near the muscle, with which the second collateral makes connexion, may also be a motor nerve cell to this musculature, but the phenomenon of the axon reflex does not of necessity imply this, for it would occur equally well if this nerve cell was an inhibitory cell to this musculature or indeed if it supplied motor or inhibitory nerves to some other musculature.

The segmental cranial nerves, which form the mesosomatic groups, are the 7th, 9th, and 10th nerves, and all these nerves supply connector fibres to peripheral ganglia, similarly to the segmental nerves already considered. Apart from ganglion cells on the œsophagus, to which the glossopharyngeal apparently sends connector fibres as well as the vagus, we have still for consideration such ganglia as the submaxillary, the otic and the spheno-palatine (Fig. 6).

The secretory fibres to the parotid gland, equivalent to the motor fibres of involuntary muscle, arise from nerve cells in the otic ganglion, and the connector fibres to these cells pass out in the glossopharyngeal nerve and travel by way of the nervus tympanicus and lesser superficial petrosal nerves to the otic ganglion.

The secretory fibres to the submaxillary and sublingual glands arise from the submaxillary and sublingual ganglia, and their connector fibres pass out in the facial nerve and travel by way of the chorda tympani to these ganglia.

The spheno-palatine ganglion supplies motor and secretory fibres in the palatine nerves to unstriped muscle and glands in the region of the palate, and the connector fibres, with which it is connected, run in the facial outflow by way of the great superficial petrosal nerve. They also supply secretory fibres to the lachrymal glands.

An outflow of connector fibres to neurons of the involuntary system has therefore occurred in all the mesosomatic segmental nerves.

In summing up the results of this chapter, we see that the motor nerve cells, which are connected with the central nervous system by bulbar and sacral connector nerves, supply with motor fibres a well-defined system of unstriped muscles, which are situated just under the lining surface of the alimentary canal and its diverticula; a system to which the name endodermal may be legitimately applied. The motor cells of this endodermal

system are found close against the muscles themselves, whether they have travelled out from the bulbar or the sacral regions, whether they are supplying with motor fibres the endodermal muscles in the small or large intestines, in the bladder, in the lungs or in the liver (Fig. 5).

Just as the sympathetic vasodermal musculature has invaded the endodermal musculature to form the sphincter of the gut, so also has the endodermal musculature invaded the vasodermal musculature in the case of the heart, as described on p. 80.

In the last chapter I pointed out that the sympathetic or vasodermal musculature formed a natural group, because the motor activities of those muscles were alone picked out by adrenalin. Now Dale has found that a substance obtained from ergot, which Ewins working with him has identified as acetyl-choline, when injected intravenously in very minute doses, produces the same effects as stimulation of the bulbo-sacral connector nerves; just as adrenaline injected intravenously in very minute doses produces the same effects as stimulation of the thoracico-lumbar connector nerves. Considering then at present only the motor actions produced by acetyl-choline, we see that it picks out the endodermal musculature just as adrenaline picks out the sympathetic or vasodermal musculature.

I conclude that, in considering the nature of the innervation of involuntary muscle, it is wrong to look upon all unstriped muscle as of the same kind; the unstriped musculature must be classified into groups, which differ from each other morphologically and also in all probability histologically; thus, as already mentioned, Kalischer looks on the vasodermal musculature as different in structure to the endodermal musculature, judging from the structure of the bladder.

Before proceeding to discuss the evidence for a system of inhibitory nerve cells and nerve fibres and glandular nerves, it will be well to sum up the conclusions already arrived at with respect to the purely motor part of the involuntary nervous system. They may be stated broadly as follows:—

The motor cells of the involuntary muscles have left the central nervous system to form the various peripheral cell groups, while the motor cells of the voluntary system have remained in the central nervous system; the axons from these latter form the ordinary motor nerves of striated muscles, the axons from the

former form the motor nerves of involuntary or unstriped muscle. The voluntary motor nerve cells are connected with the connector nerve cells by connector nerve fibres. These connector fibres give off collaterals and so connect the higher centres with a number of voluntary segments. The involuntary motor nerve cells are likewise connected with higher centres by connector nerves, the fibres of which give off collaterals and so connect the higher nerve centres with a number of involuntary segments. In the latter case these connector nerves are naturally partly within and partly without the central nervous system. Those parts, which run free of the central nervous system to the vagrant motor cells, form part of such nerves as the vagus nerve, the rami communicantes of the sympathetic system and the pelvic nerve. These connector nerves of the involuntary nervous system have left the central nervous system in three main outflows, a bulbar outflow known as the vagus system, a thoracico-lumbar outflow known as the sympathetic system, and a sacral outflow, the pelvic system. These three outflows are separated from each other by the interpolation of segments belonging to the voluntary system, which are especially developed owing to the formation of the vertebrate limbs.

The three outflows differ in function in a striking manner. The motor cells of the sympathetic system send motor fibres to the muscles of the heart and of the blood vessels over the whole body, and to a system of involuntary muscles, which possibly arose from a system of dermal muscles situated just under the skin over the whole body.

The motor cells of the vagus and pelvic systems send motor fibres to a system of involuntary muscles belonging to the alimentary canal and its derivatives, a system of endodermal muscles, the vagus group being confined to the small intestine and its derivatives, and the pelvic group to the large intestine and its derivatives.

The connector nerve cells whose axons form connector fibres to the motor neurons are all situated in the central nervous system, but, owing to the difference of position of the motor neurons of the involuntary nervous system as compared with those of the voluntary nervous system, the connector nerves of the involuntary nervous system pass out of the central nervous system and thus form the efferent part of such nerves as the vagus and pelvic nerves.

We see that not only is the involuntary nervous system built up on the same plan as the voluntary nervous system, but also it innervates a double arrangement of unstriped musculature of the same character as the double arrangement of striated musculature seen in the somatic and splanchnic segmentations; for clearly the unstriped muscle under the skin, which forms the sympathetic or epidermal musculature, belongs to the somatic segmentation, and equally clearly the endodermal musculature belongs to the splanchnic segmentation. Naturally, on the theory put forward by me of the origin of vertebrates, the original animal, from which the vertebrates arose, possessed a double segmentation throughout its whole length; a body segmentation and an appendage segmentation. The muscles of these two segmentations, derived originally in the segmented annelids from unstriped muscle, became in part striated and voluntary and partly remained unstriped. The unstriped muscles of the somatic segmentation form the sympathetic or epidermal musculature, and those of the appendage segmentation the endodermal musculature, which groups directly with the endodermal striated musculature of the mesosomatic region. The motor neurons of these two musculatures show a corresponding differentiation and agreement with those of the striated muscles. The motor neurons of the unstriped muscles belonging to the somatic segmentation are the motor cells and motor fibres of the so-called sympathetic system, which were originally in close contiguity with the posterior root ganglia of the spinal nerves, belonging to the somatic segmentation; while the corresponding motor neurons of the splanchnic segmentation are the motor cells and motor fibres of the 'enteral'* system, which were originally in close contiguity with the posterior root ganglia of the bulbar and sacral nerves, belonging to the splanchnic segmentation. Finally, the involuntary muscles of these two segmentations are most markedly differentiated from each other by the action of adrenaline on the one hand, which causes contraction of the vasodermal or sympathetic system of muscles, and of acetyl-choline on the other, which causes contraction of the endodermal system of muscles.

* A well-defined system of nerve cells and nerve fibres is understood universally by the term sympathetic nervous system. As we have seen, the main characteristic of the nerve cells of this system is to send motor fibres to the vascular and dermal muscles. At present there is no term to express that similar nervous system, the main characteristic of which is to send motor fibres to the endodermal muscles. I propose to call it the 'enteral' nervous system.

CHAPTER IV

THE CHARACTERISTIC MOTOR FUNCTIONS OF THE NERVE CELLS BELONGING TO THE MID-BRAIN OR PROSOMATIC OUTFLOW OF CONNECTOR NERVES

THE final outflow of connector nerves to be considered is that in the prosomatic group of segmental cranial nerves.

This prosomatic group, which is comparable with the nerves of the segments of the prosoma in such an animal as Limulus, includes the 3rd, 4th and 5th cranial nerves, and just as my anatomical researches in 1885 demonstrated an outflow of fine medullated fibres in the mesosomatic group of nerves, so also I found masses of small medullated fibres in certain roots of the prosomatic group of nerves. These were especially visible in the roots of the 3rd nerve, and following them out along the nerve I found they left it to enter into the ciliary ganglion (Fig. 6). A series of sections through the ciliary ganglion showed that no large medullated fibres, such as are characteristic of the sensory fibres of the fifth nerve, were in connexion with the cells of this ganglion ; any such fibres could be traced through the ganglion without connecting with any of the nerve cells. It was then quite certain that this ganglion was not of the nature of a posterior root ganglion, as had often been asserted by comparative anatomists. From this ganglion the short ciliary nerves proceed to supply the sphincter muscle of the iris and the ciliary muscles with motor fibres ; these observations made it certain that the cells in the ciliary ganglion were motor cells to these involuntary muscles of the eye. This conclusion was subsequently confirmed by Langley and Anderson by the use of nicotine and the method of degeneration.

I noticed at the same time a striking peculiarity of the motor fibres from this ganglion, for they were all medullated, not non-medullated as is usual in the motor fibres from the sympathetic nerve cells. We have then here, in the ciliary ganglion, a

system of motor neurons which resemble those of the voluntary system, in that their axons are all medullated, although the muscles they supply are not striated. Now in the birds, the corresponding muscles are striated, and Anderson has found that in this case their motor cells are still in the ciliary ganglion, but the axons of these cells are now large medullated fibres resembling those to other striated muscles. Also the connector fibres from the central nervous system to these cells are large.

I conclude then that, when the motor neurons to a muscle have once passed out from the central nervous system to form a peripheral ganglion, they cannot go back into the central nervous system even though the muscle take on the type of those belonging to the voluntary system.

I do not think this muscular system ought to be included in either of the groups of involuntary muscles already considered. The marked medullation of its motor nerves and the striation of its fibres in birds place it in a separate category as something intermediate between unstriped and striated muscle; its nearest ally is the endodermal musculature, but it is difficult to see how it could have arisen from that group. It is significant in this respect that Dale could not find any effect upon the pupil by the injection of acetyl-choline.

The innervation of another muscle of the eye may now be discussed. The dilatator muscle of the mammalian pupil forms a layer of radially arranged muscle fibres below the posterior limiting membrane of the iris, which are so covered with pigment that for a time it was disputed whether they were muscle fibres at all, and whether the dilatation of the pupil upon stimulation of the cervical sympathetic was not brought about through the relaxation of the fibres of the sphincter muscle by stimulation of inhibitory nerve fibres. Langley and Anderson however settled this question by cutting a radial strip of the iris and showing its shortening upon stimulation; he also caused a deformation of the shape of the iris upon stimulation at the edge of the sclerotic in the intact eye, especially at the places where the long ciliary nerves enter the iris. These peculiar, pigmented, radially arranged cells therefore are muscular in nature. Their motor cells are situated in the superior cervical ganglion and their motor fibres reach the muscle by way of the long ciliary nerves. I conclude that the dilatator muscle belongs to the system of dermal muscles, its motor neurons are

situated in the superior cervical ganglion and the connector fibres leave the spinal cord in the uppermost thoracic anterior roots; adrenalin here produces its characteristic effect.

There are in the bird's eye well-defined radial striated muscles, which form the dilatator muscle of the pupil, in addition to the striated muscles which correspond to the unstriped sphincter and ciliary muscles in the mammalian eye. The innervation of these has been investigated by Zeglinski, who states that their motor nerves are not in the cervical sympathetic but run to the muscle direct in the *ramus ciliaris*, which arises from the first or ophthalmic branch of the trigeminal. When however we consider that the ophthalmic branch of the trigeminal is in all vertebrates a purely sensory nerve, it does not seem likely that these motor fibres belong to it; it is much more probable that they have come into the *ramus ciliaris* from some other source. Two possibilities present themselves, either that, as in the mammal, these motor fibres arise from cells in the superior cervical ganglion—which is denied by Zeglinski—or that they come from cells in the ganglion stellatum, and reach the trigeminal by way of the *ramus vertebralis*. It is not absolutely clear whether the striated dilatator muscle of the bird is homologous with the same muscle of the mammal. Grunhagen states that a radial pigmented structure, similar to that in the eye of the mammal, is present in the bird's eye in addition to the striated dilatator muscle; he did not however recognize the muscular character of these radially arranged pigmented cells in the mammal any more than in the bird.

With the consideration of the motor cells in the ciliary ganglion, I have now completed the survey of all the outflows of connector fibres to motor nerve cells belonging to the involuntary nervous system.

CHAPTER V

THE INHIBITORY NERVES

So far I have built up the conception of an involuntary nervous system formed on the same plan as the voluntary nervous system, but with its motor nerve cells outside the central nervous system. We come now to a much more difficult question, the meaning of inhibition in these two systems. In the voluntary nervous system we are accustomed to the conception of inhibition of motor activities in connexion with co-ordinated actions, and consider such inhibition to be brought about by interaction between parts of the central nervous system itself, i.e. through impulses passing along connector nerves of the voluntary system. An exactly similar inhibition might be produced in the involuntary nervous system by impulses passing along connector nerves of the involuntary system; in other words, by stimulation of nerves like the vagus, the splanchnic, and the pelvic nerves. In the voluntary nervous system we cannot go farther than this; all the fibres which pass to muscles from the cells of the anterior horn are motor in function, and, what is more important, there is no evidence of more than one nerve fibre ending in a muscle fibre, so that neither histologically, nor physiologically, is there any evidence for the existence of nerve cells among the anterior horn cells, which give origin to fibres inhibitory to the contraction of voluntary muscle.

In the involuntary system on the contrary we cannot refer all cases of inhibition to the action of connector fibres, for there seems to me clear evidence that the fibres passing from certain nerve cells to the tissue itself are not motor but inhibitory to the activity of that tissue; we must in fact accept, in the case of the involuntary nervous system, the existence of inhibitory cells and fibres, as well as motor cells and fibres.

The question is: Is there evidence that fibres which relax contracted involuntary muscle pass directly into that muscle

from inhibitory nerve cells, just as fibres which contract involuntary muscle pass directly into the muscle from motor nerve cells?

It is well known that stimulation of the lumbar splanchnic nerves causes relaxation of the musculature of the bladder, and that the fibres concerned end in cells of the inferior mesenteric ganglion; also that from these same cells fibres pass to the bladder muscle itself, and cause relaxation of the detrusor urinæ, as is seen upon stimulation of the hypogastric nerve. Such cells are, according to my view, inhibitory cells, giving off inhibitory fibres directly to the muscle itself; and the actual proof that these nerve fibres induce chemical changes of this nature in the muscle is given by the action of adrenaline; for adrenaline not only causes relaxation of the bladder musculature in the normal condition, but also, as Elliott has shown, relaxation of the decentralized bladder, and still more markedly of the denervated bladder. In order to denervate the bladder completely he removed with the help of a lens all the nerve cells lying on the surface of the bladder, and six weeks afterwards applied adrenaline. This caused relaxation of the bladder, but no effect was caused by stimulation of either the pelvic or hypogastric nerve. This action of adrenaline on the denervated muscle, which is the same as that caused by stimulation of the hypogastric nerves, seems to me proof positive that these fibres of the hypogastric nerve are inhibitory right into the muscle substance itself, and that therefore involuntary nerve cells can give rise to inhibitory nerves as well as motor nerves.

I shall then speak of inhibitory nerves as well as motor nerves and of inhibitory as well as motor cells, without implying that they are always separate from each other, admitting, that is the possibility that a single nerve cell can give off both inhibitory and motor fibres.

The first question that requires an answer is: Have the inhibitory nerve cells of any particular muscular system travelled out from the central nervous system in the same outflows as the motor nerve cells of that system?

I will consider the vascular system separately and take first the dermal system, the motor cells of which are found in the ganglia of the lateral sympathetic chain. To this system belongs the retractor penis muscle, an unstriped muscle which is inserted

at the attachment of the prepuce and is continued backwards in the middle line over the ventral surface of the corpus spongiosum and bulbus urethræ. Langley and Anderson have shown that stimulation of the pelvic nerve causes relaxation of this muscle, while, since it belongs to the dermal system, its motor cells are situated in the lateral chain of ganglia of the sympathetic system, the particular ganglia involved being, according to Langley, in the cat and dog the three sacral ganglia: the motor fibres from these ganglia reach the muscle by way of the pudic nerve. The cells on the pelvic nerve, with which the inhibitory fibres are connected, are situated in the neighbourhood of the retractor muscle itself.

In precisely the same manner the unstriped musculature around the anus and in the perineal region, which also belongs to the dermal system and receives motor fibres from cells in the lateral chain, according to Langley and Anderson relaxes on stimulation of the pelvic nerve: these inhibitory cells again are situated in the neighbourhood of the muscles. We see then that, as far as these few muscles of the dermal system are concerned, their inhibitory cells have not travelled out in the same outflow as their motor cells, but in the same outflow as the motor cells of the endodermal musculature of the cloaca.

In the case of the rest of the dermal system, namely the whole pilo-motor group, the musculature of the sweat glands, etc., we have at present no knowledge of any inhibitory fibres at all.

The next group for consideration is the genitodermal group of muscles, the motor nerve cells of which have travelled out in connexion with the thoracico-lumbar outflow, and are situated almost all, if not all, in the neighbourhood of the musculature itself. The evidence for the existence of inhibitory nerves to this system is based largely on the action of adrenaline, after ergotoxine has been given.

Dale has obtained from ergot a substance to which he has given the name ergotoxine, which possesses the remarkable property of paralyzing only the motor nerves of the sympathetic system; so that in the case of a particular muscle group, which is supplied with motor and inhibitory fibres by a combined sympathetic nerve, and in which stimulation or the application of adrenaline normally gives only motor effects, after the injection of

ergotoxine stimulation or adrenaline will produce inhibition, not contraction. By this means the presence of inhibitory nerves has been detected in many cases. The presence of inhibitory nerves to the musculature of the uterus has thus been demonstrated by Dale, who has shown that they pass to the uterus along the hypogastric nerves, having passed out of the spinal cord in the lumbar splanchnics. He has shown that in the virgin uterus of certain animals inhibition is the normal effect of either stimulating the hypogastric nerve or of giving adrenaline, while in the pregnant uterus the normal effect is contraction, which can then be converted into inhibition by paralyzing the motor fibres with ergotoxin. The motor and inhibitory neurons for the uterus have therefore travelled out together, and are both found in the groups of cells situated in the neighbourhood of the uterus.

In the urodermal group we have also especially to consider the ureters, in which similar groups of nerve cells have been described by Protopopow. The connector fibres to these nerve cells run in the hypogastric nerves, and Fagge has shown that stimulation of the hypogastric nerve in the dog is always followed by a motor effect on the ureter, which is evidenced either by a quickening of the normal rhythm of contraction, by the production of groups instead of single contractions, or by the production of groups of contractions in a previously quiescent ureter. Elliott has given evidence of an inhibitory action on the muscles of the ureter in the dog upon the application to the ureter of adrenaline, 1 in 2000. Neither the uterus nor the ureter is innervated in any degree from the sacral outflow.

I conclude that both the inhibitory and motor nerve cells of the urogenito-dermal system have travelled out together in the thoracico-lumbar outflow right up into the organs themselves, and their connector fibres reach these cells by way of the lumbar splanchnics and the hypogastric nerves.

We come finally to the most interesting group, the sphincter or sympathetic musculature of the gut, and with it we will consider also the inhibitory fibres for the sacral and bulbar endodermal musculature.

In the sphincter musculature of the cloacal region of the gut I have included the internal sphincter ani and the sphincter of the bladder and urethral muscles. The motor nerve cells for all

these muscles are situated in the inferior mesenteric ganglia, except a few outlying cells for the internal sphincter ani (Fig. 7). According to Elliott, stimulation of the pelvic nerve causes in the rabbit relaxation of the urethral muscles and sphincter of the bladder and also of the internal sphincter ani. The inhibitory cells for these muscles have therefore travelled out in the sacral outflow, while their motor cells belong to the thoracico-lumbar outflow. On the other hand, stimulation of the lumbar splanchnics or of the hypogastric nerves or the application of adrenalin causes inhibition of the endodermal musculature both in the bladder and the large intestine, the nerve cells, from which these inhibitory nerves arise, being situated in the inferior mesenteric ganglion.

We see then that the motor cells of the sphincter (sympathetic) muscles of the vesical and intestinal portions of the cloaca have travelled out with the inhibitory cells of its endodermal vesical and intestinal muscles, and are found together in the same ganglion.

Conversely, the motor cells of the cloacal endodermal muscles are found in the vesical and rectal plexuses and, as already mentioned, inhibition of the sphincter muscles of this region is brought about by stimulation of the pelvic nerve, the connector fibres of which connect with cells in the same plexuses. Thus the motor cells of the cloacal endodermal muscles have travelled out with the inhibitory cells of the sphincter (sympathetic) muscles of the vesical and intestinal portion of the cloaca, and are found together in the same ganglionic plexus.

Passing now to the region of the small intestine we find, as might be expected, the same kind of phenomena as in the large, substituting only superior mesenteric ganglion for inferior mesenteric ganglion, and the vagus nerve for the pelvic nerve. Thus the thoracic splanchnics inhibit the endodermal musculature of the small intestine and cause contraction of the sphincter (sympathetic) musculature, namely, the ileo-colic and possibly the pyloric sphincters, the nerve cells in both cases being situated in the superior mesenteric ganglion. The motor cells of the sphincter (sympathetic) muscles of the small intestine have therefore travelled out with the inhibitory cells of its endodermal musculature, and are found with them in the same ganglion—the superior mesenteric ganglion.

Conversely, the motor cells of the endodermal musculature are found in Auerbach's plexus, and stimulation of the vagus

nerve ought to cause inhibition of the ileo-colic and pyloric sphincters, but here our information is lacking. Elliott has not been able to find any evidence of any action of the vagus nerve on these muscles. There is this only to be said: if it is true, as Dixon asserts, that in the case of the stomach of the frog the sympathetic system of muscles is the main system, so that stimulation of the thoracic splanchnic causes contraction of the stomach, then, seeing that he states at the same time that stimulation of the vagus causes relaxation, there is evidence that the vagus nerve does cause inhibition of the sympathetic musculature in this region, just as it ought to do.

With respect to the internal sphincter of the anus it does not appear that all its motor cells are situated in the inferior mesenteric ganglion, for its contraction reflexly on stimulation of that end of the cut hypogastric nerve which is connected with the inferior mesenteric ganglion—the so-called axon reflex—implies the existence of motor cells, either on the course of the hypogastric nerve, or close to the muscle itself. It is suggestive, with respect to the position of these cells, that Dale has found that after the administration of ergotoxine, either stimulation of the peripheral end of the hypogastric nerve or the application of adrenaline causes a relaxation of the muscle, so that these outlying sympathetic motor nerve cells are accompanied by outlying sympathetic inhibitory nerve cells. From these two observations of Elliott and Dale it would appear that the internal sphincter ani muscle is composed of two parts, of which one is supplied by motor and inhibitory neurons, which have travelled out together in the thoracico-lumbar outflow and are situated near the muscle, and the other is supplied by motor neurons belonging to the thoracico-lumbar outflow and situated in the inferior mesenteric ganglion, and by inhibitory neurons belonging to the sacral outflow.

The exact point in the upper alimentary canal, where all influence of the sympathetic nerve ceases, is a doubtful point. All observers agree that the splanchnic nerves do not affect the œsophagus, either in the direction of contraction or inhibition. Both motor and inhibitory nerves in this region belong to the vagus outflow. Somewhere in the stomach is the termination of the sympathetic nerve supply. Now Cannon has shown that the cardiac end of the stomach is a receptacle for holding food, and that the active churning movements are confined to the antrum

and commence at a marked line of constriction between the cardium and the antrum which is known as the incisura cardiaca. According to his investigations the cardiac end of the stomach, inclusive of the cardiac sphincter, is innervated by both motor and inhibitory fibres in connexion with the vagus nerve alone, while the pyloric end has a sympathetic as well as a vagus supply. The present evidence therefore points to the incisura cardiaca as the upper limit of the sympathetic supply.

The peculiarities of the innervation of the muscular tissues of that part of the alimentary canal between the stomach and the anus point distinctly to the derivation of its musculature from two distinct sources. The one (Fig. 5) which is endodermal, has arisen from a musculature connected anteriorly with that of a respiratory chamber, to the motor cells of which the vagus nerve supplies the connector fibres, and connected posteriorly with that of a cloacal chamber, to the motor cells of which the pelvic nerve supplies the connector fibres; the other (Fig. 7) has arisen from a musculature, possibly dermal originally, the motor cells of which are situated in the inferior and superior mesenteric ganglia of the sympathetic, and are connected with the central nervous system by connector fibres in the thoracico-lumbar outflow. Possibly both musculatures originally extended from the stomach to the anus, and with the elongation of the gut the sympathetic musculature became more and more confined to those places, where sphincter muscles were a physiological necessity. The innervation of these two musculatures gives the best example of reciprocal innervation it is possible to conceive, for the motor neurons to the one musculature are always found in close contiguity with the inhibitory neurons of the other, and vice versa.

Such is the nature of the evidence for the existence of inhibitory nerves and nerve cells for the unstriped musculature of the vertebrate apart from that of the vascular system. Further light is thrown upon the question of inhibition and reciprocal innervation by the study of the nervous system of the invertebrate, especially by investigations into the mechanism concerned with the opening and closing of the claw of the crayfish. Richet noticed that stimulation of the nerves in the limb of the crayfish caused opening of the claw if the stimulus was weak, and closing of the claw if the stimulus was strong. Biedermann described the two muscles concerned, a short strong ad-

ductor muscle and a weaker abductor, and found that removal of the one muscle produced a condition of tone in the other. With well-pronounced tone in the adductor he found that weak stimulation produces inhibition of the tone of the muscle and the claw opens, strong stimulation produces contraction and closure of the claw. On the other hand with the abductor muscle isolated and in a condition of tone, weak stimulation causes contraction of the muscle and the claw opens, while strong stimulation causes inhibition and the claw closes. The same strength of stimulus, which causes contraction of the one muscle, thus causes inhibition of the other. The stimulus was always applied by electrodes stuck into the limb itself, so that, on the assumption that inhibitory nerves exist apart from motor nerves, each stimulus stimulated four nerves simultaneously. In the case of the adductor muscle the inhibitory fibres are stimulated more strongly than the motor fibres when the stimulus is weak, by increase of strength of stimulus the motors get the upper hand, while in the case of the abductor muscle the motors are supplanted by the inhibitors with a strong stimulation.

The nerve to the appendage divides into two nerves immediately after it leaves the central nervous system, as is shown in Hardy's paper (cp. his figures 11 and 12). Of these two nerves one is larger than the other, and Marshall found in Homarus vulgaris that, if the larger nerve was cut and its distal end stimulated, the claw closed, whereas if its central end was stimulated, the claw opened reflexly; with the smaller nerve he obtained the opposite results. Hardy confirms this for *Astacus*. The larger nerve then is the adductor motor nerve, the smaller the abductor motor nerve. With these two nerves Celesia has repeated Biedermann's experiment and found that, when the abductor muscle is cut away, stimulation of the abductor nerve causes inhibition of the adductor muscle and vice versa, so that the motor nerve of the one muscle leaves the central nervous system with the inhibitor nerve of the opposing muscle.

Now the motor nerve consists of fibres which are undoubtedly the axons of some of the large nerve cells so conspicuous in the crustacean nervous system. Where do the inhibitory fibres come from? Unfortunately at present we do not know sufficiently the structure of the central nervous system in the crustacea to give a definite answer to this question, but there are certain significant

peculiarities which I think worth pointing out in the hope that subsequent research will decide the value of these signposts. The most thorough and detailed account of the structure of a ganglion in Astacus, is that given by Hardy. He points out that three pairs of nerves arise from each of the first five abdominal ganglia :—

1. An anterior pair which arise directly from the ganglion and contain a large number of the fine or afferent fibres and comparatively few of the larger or efferent fibres. These supply the appendages with motor and sensory fibres and also the skin of the sternum and pleura.

2. The posterior ventral nerves containing relatively more large fibres. These supply the dorsally placed extensor muscles of the segment and the dorsal skin in the next following segment.

3. Posterior dorsal nerves which are purely motor and innervate the flexor muscles of the segment.

The motor fibres in these nerves are very large and few, and each arises from a large motor cell in the ganglion. Thus in the second abdominal ganglion the posterior dorsal nerve consists of only ten large fibres which innervate all the flexor muscles of that segment. Each of these large fibres divides repeatedly on its way to the muscles, ultimately splitting into many small fibres which reach their destination in the muscles themselves. In fact each motor nerve cell and fibre resembles the large motor cell and fibre of the torpedo electric organ, which itself is a modification of a muscular mass. This appears to be the rule in the crustaceans and annelids ; a single large cell in the central nervous system innervates a large number of muscles by the brush-like splitting up of its large axis cylinder process. The process of evolution has brought about the large brain development of the vertebrate, and the greater niceties of voluntary movement have necessitated the more separate innervation of muscle fibres by the smaller cells of the anterior horn. Again in this instance, embryology, as is always the case, recapitulates the phylogeny and shows how with the proliferation of the muscles of the myotomes, there is a splitting up of their motor nerves to form a brush-like termination supplying the rapidly proliferating muscles.

The most beautiful and clear evidence of this process is given by Miss Alcock's discovery. The adult lamprey Petromyzon possesses a large and elaborate sucking apparatus which consists

essentially of a sucking disk with a very powerful muscle, the basilar muscle, and a long piston or tongue with powerful muscles attached to it. The larval form or Ammocœtes shows no sign of any such apparatus, this is formed with great rapidity at the time of transformation. Miss Alcock has shown that the motor nerves to these suctorial muscles, which belong to the trigeminal nerve, are present in the Ammocœtes and supply certain embryonic cells which are found in the tentacles and lower lip. At transformation these cells proliferate amazingly and form muscle fibres, but the nerve fibres in the branches of the trigeminal do not increase in number until they are near the proliferating muscle cells, when they split into an enormous number of brush-like filaments in correspondence with the enormous proliferation of the embryonic muscle cells. Each trigeminal motor nerve fibre and the cell in the trigeminal nucleus, from which it arises, becomes very large in size, so that in this trigeminal motor system of Petromyzon we see the same phenomena as is so common in the invertebrate nervous system, namely, large motor nerve cells with large axons which split peripherally into a brush of smaller nerve fibres and so supply a large number of muscle fibres.

Another most important conclusion results from these investigations of Miss Alcock; they give no support to the theory of His that in the early embryo the muscle cell is not connected with its motor nerve cell, but that the motor fibre is formed by the growing out of a process from the neuroblast which finally reaches the forming muscle cell, and becomes attached to it. In the Ammocœtes during the larval stage, which constitutes the greater part of the life of the animal, the embryonic motor fibres are there although the muscles are not definable as such, but their cells are in that so-called indifferent embryonic condition, when according to His the processes from the neuroblast could not yet have reached them.

The further evolution of the nerve supply to the voluntary muscles of the vertebrate is I imagine that the splitting process finally involves the nerve cells themselves, and thus forms the comparatively small cells of the anterior horn.

Another very striking peculiarity of some of these large motor cells of invertebrates, especially manifest in Annelids, has been described by Retzius and others, having been demon-

strated by the methylene blue method. The axons of many of them are seen to divide while still in the central nervous system, thus forming two nerve fibres one of which is usually larger than the other: the one fibre passes out into one nerve while the other passes into another nerve. The one fibre passes out as the large motor fibre to a group of muscles, the other passes into a nerve which supplies with motor fibres the opposing musculature—if we may judge from Hardy's researches on the motor nerves to the flexor and extensor muscles and Celesia's work on the two nerves which supply respectively the opening and closing muscles of the claw with motor fibres. Such a nerve fibre can hardly be a motor fibre but may possibly be an inhibitory nerve fibre to the opposing muscle.

The only evidence which I know in the vertebrate kingdom of the axon of a presumably motor neuron dividing into two fibres, which travel to different destinations, is given by Dogiel in the case of some of the cells of Auerbach's plexus. The cells of Auerbach's plexus are arranged in groups along the intestine and, as already mentioned, nerve fibres coming from elsewhere (vagus in my opinion, sympathetic according to Dogiel), make connexion with many of these ganglia by means of collaterals; further these groups of nerve cells are generally considered to consist of motor neurons so that their axons are motor axons. The connector fibres to these cells and their motor fibres form a mesh-work of nerve fibres which is so marked a feature of Auerbach's plexus. If in this mesh-work two sets of motor fibres cross each other on their way to the muscles of the intestine, then it is clear that the one set of motor fibres will in all probability innervate a different part of the musculature from that of the other set. Now Dogiel points out, that among these nerve cells of Auerbach's plexus, certain cells exist, each of which has an axon which passes undivided along a strand of fibres until it reaches the junction point with another strand; it there splits into two fibres which pass to their destination, one along one strand and the other along the other. If these are, as seems probable, motor axons, then we have here a most suggestive resemblance to a common occurrence among invertebrates, which must be taken into account in the consideration of reflex action in the isolated intestine. The further consideration of this question will be taken in a later chapter.

CHAPTER VI

THE INHIBITORY NERVES TO THE VASCULAR SYSTEM

I TURN now to the question of inhibitory nerves to the vascular system, and I will consider in the first place the innervation of the heart. It is universally recognized that the cardiac fibres of the vagus nerve are inhibitory in action, that they enter the heart as medullated fibres and connect with nerve cells in the heart itself. After nicotine has been given these fibres no longer produce any effect, though at the same time the non-medullated augmentor nerves, which reach the heart from sympathetic ganglia, are still able to cause the same action as before the nicotine was given ; from this fact the conclusion may be definitely drawn, that all the nerve cells in the heart belong to the vagus group and none to the sympathetic. The action of nicotine thus enables us to draw a conclusion similar to that in the case of Auerbach's plexus in the small intestine; all the cells belong to the vagus nerve and none to the sympathetic.

Further the investigations of Dogiel, by means of methylene blue staining, on the nerve structures in the heart show that these medullated fibres connect up with various groups of ganglion cells in the heart by means of collaterals, so that the cardiac vagus fibres fall into line with the rest of the connector nerve fibres belonging to the involuntary system, and are in reality connector fibres to the cardiac nerve cells.

Finally His junior has shown that in an early condition of the embryo the cardiac nerve cells have not yet reached the heart but are found outside it ; with the growth of the heart they become included in it. He concludes that they have passed out from the central nervous system to reach the heart, and are not found in the heart itself from the beginning. These cardiac nerve cells behave then in all respects like the sympathetic nerve cells, and demonstrate the uniformity of origin of all the peripheral nerve cells belonging to the involuntary nervous system.

Both Kuntz and Miss Abel agree with His junior that the cardiac cells have come into the heart from outside, and both trace them from cells belonging to the vagus which were at first close against its root ganglia and afterwards have travelled out to the heart. They both state that only vagus cells have thus travelled into the heart.

Do the cardiac nerve cells also supply motor nerves to any muscle? Is there any evidence of two kinds of muscle in the heart similar to the evidence I have given of two kinds of muscle in the gut? There certainly is evidence, and it is of a most striking kind.

Fano in 1900 found that, when records were taken of the contractions of the auricle and ventricle of the water tortoise, *Emys Europæa*, a clamp being placed at the auriculo-ventricular groove, the base line of the auricular tracing was not straight but slowly undulating, the rhythm of the waves being often remarkably regular. The auricle of this tortoise shows the presence of two rhythmical activities going on simultaneously, the one a tonic rhythm having the appearance of Traube-Hering curves, and the other the ordinary heart beats superimposed on this tonic rhythm. Fano at first looked upon this phenomenon as indicating the presence of two kinds of muscle in the auricle, the one the ordinary quickly contracting cardiac muscle and the other a more slowly contracting kind, which in consequence of the clamp in the auriculo-ventricular groove was set into rhythmic action. He drew attention to the fact that atropine removed these rhythmic tonic contractions while the heart beats continued, but muscarine removed the heart beats while the tonic rhythm continued. Bottazzi found evidence of the same kind of phenomenon in Amphibia, and in tortoises other than *Emys Europæa*, but always to a less extent than in *Emys Europæa* itself; and Rosenzweig, working with Engelmann, found that the clamp at the auriculo-ventricular groove was not necessary for the production of this tonic rhythm, but that bloodlessness and a dying condition of the heart were sufficient to bring about the phenomenon. Thus, whereas in a freshly put up heart there might be no trace of rhythmic tonic contractions, the same heart exhibited the phenomenon strongly on the next day. Rosenzweig further examined the auricle of *Emys Europæa* histologically, and found that close against the endothelium was a layer of muscular tissue

in which no striation could be seen. He ascribed the tonic rhythmical contractions to the contractions of this layer. Bottazzi found the two kinds of contraction behaved differently to stimulation of the cardiac nerves; stimulation of the augmentors inhibits these tonic contractions so that the auricular beats now all start from the same base line, while, of course, the beats are themselves increased in strength; conversely stimulation of the vagus will make the tonic rhythm appear, if it is not present, and increase the strength of the waves if they are weak, while, as is well known, it diminishes the strength of the auricular beats. Rosenzweig has been unable to confirm these statements of Bottazzi, so far at all events as the vagus is concerned.

At the same time Bottazzi's statements agree in a remarkable way with Fano's observation upon the action of atropine and muscarine upon these two kinds of rhythm, for atropine is essentially a paralyzer of the activity of muscular structures, to which the vagus cells send motor fibres, while it leaves alone or even increases the activity of muscular structures whose motor fibres belong to sympathetic cells; and muscarine paralyzes the latter but not the former.

Since Rosenzweig's paper, Bottazzi has re-examined the question. He finds that it is not necessary to use a clamp or to bleed the animal, or to wait a long time for the appearance of the tonic rhythm in the auricle, if the animals are cooled down in an ice-chest at a temperature of 9° C. This he says is indispensable in order to be sure of obtaining auricles with a good tonic rhythm and responsive to nerve stimulation. He confirms his previous observations on the respective actions of the two cardiac nerves, and also shows that adrenaline produces the same effect upon the two rhythms as stimulation of the sympathetic. Oinuma has confirmed Bottazzi's observations on the cardiac nerves, and I have seen the same action of adrenaline as he describes upon the auricle of Chrysomis Picta, an American species allied to Emys. Bottazzi also in conjunction with Ganfini has examined histologically the auricular tissue of Emys, and has confirmed Rosenzweig's discovery of unstriped muscle fibres in the auricle. They form a strong layer next to the endothelium and continue into the sinus venosus and the beginnings of the great veins; the striated muscle fibres also continue into such a vein as the vena hepatica, always lying external to the layer of unstriped

muscle. In agreement with its histology the sinus venosus exhibits a well-marked tonic rhythm which is influenced by the cardiac nerves in the same way as that in the auricle.

These observations definitely prove the existence in the heart of a system of unstriped musculature in addition to the striated cardiac muscles, which is especially well developed in the water tortoises and extends from the auricles into the beginnings of the great veins. This unstriped muscle resembles the enteral unstriped muscles, the bronchial muscles, and those of the gall bladder in its behaviour to poisons like atropine and muscarine and in its innervation ; for all these muscles are supplied with motor fibres from cells connected with the vagus outflow, and with inhibitory fibres from cells connected with the thoracico-lumbar outflow. On the other hand the striated cardiac muscle resembles the enteral sphincter muscles, in that their motor nerve cells are connected with the thoracico-lumbar outflow, and their inhibitory cells with the vagus outflow. In fact, exactly the same kind of reciprocal innervation exists in the heart as in the intestine, and this fact suggests in the mind of the observer the same question :—were the vagus and sympathetic cardiac nerve cells, which have travelled out from the central nervous system, originally nerve cells, whose axons divided into two nerve fibres, of which the one was motor or inhibitory to the unstriped cardiac musculature, and the other inhibitory or motor to the striated cardiac muscle ? The disappearance of the unstriped muscle in the higher vertebrates would bring about the disappearance of its motor and inhibitory nerves, and leave the vagus cells inhibitory to the heart muscle, and the sympathetic cells motor or augmentor to it.

It is an extraordinary thing that such a nerve as the vagus, which is essentially the motor nerve to the striated musculature of the respiratory portions of the gut, and supplies connector fibres to the motor cells of the unstriped gut musculature, should also be connected with motor cells to any cardiac musculature ; but an explanation of the apparent anomaly is suggested when we turn our attention to the manner of formation of the vertebrate heart.

Such a method of heart formation is unique in the animal kingdom ; for the vertebrate heart is formed, as is well known, by the coming together in the mid-ventral line of two vessels

which lie originally on each side of the notochord close against the lining of the gut wall, which encloses the yolk. With this infolding, by which the throat is formed and the two parts of the heart brought together in the mid-ventral line, it is not impossible that some of the muscular structures in reality belonging to the gut may have become involved in the formation of the heart. Such an assumption would account for the supply of motor nerve cells of the vagus system to an unstriped musculature in the heart, and also for the action of atropine and muscarine on such a layer, while the varying character of the extent of this muscular layer on the vertebrates and its disappearance in the higher vertebrates would account for the final condition, in which only motor or augmentor fibres from the cells of the sympathetic system and inhibitory fibres from the vagal cells remain.

In close connexion with this question of the presence of inhibitory nerve cells and nerve fibres to only certain muscular tissues in the heart, is the striking difference between different animals in the behaviour of their hearts to stimulation of the vagus nerve ; for whereas the inhibitory action of the vagus can be demonstrated on the muscular tissue of the sinus, auricles and ventricle of all the Amphibia, such action is confined to the musculature of the sinus and auricles in the Reptilia. This statement is founded on the behaviour of the tortoise, snake and crocodile, in none of which have I ever seen any inhibitory effect on the ventricular muscle produced by stimulation of the vagus nerve. In this respect the mammalian heart behaves like the amphibian, and the avian like the reptilian. According to McWilliam the eel's heart behaves like that of the tortoise. The meaning of this strange difference in various vertebrate hearts which have been investigated is a very difficult problem and will be discussed later.

The nerve cells in the heart are everywhere associated with the course of the vagus fibres ; thus in the frog the cells known as Remak's ganglia are massed, where the fibres first enter the heart along the superior vena cava ; again in connexion with the two vagus nerves in their course along the auricular septum we find the inter-auricular ganglia or Ludwig's ganglia, and finally the vagus nerves terminate in the two ganglia at the auriculo-ventricular junction, known as Bidder's ganglia. A few ganglion cells have been found by Dogiel and others in the

ventricular tissue and along the nerve fibres passing to the auricles from the sinus, namely the auriculo-ventricular junction or inter-auricular nerves. The main mass of the auricular or ventricular muscles as well as the muscles of the bulbus arteriosus are free from nerve cells.

We find further that when, as in the tortoise, the fibres of the vagus nerves in their passage from the sinus to the ventricle do not travel in the septum between the two auricles, there are no nerve-cell groups in the septum, the nerve cells being only found in connexion with the nerve fibres. I conclude that all the nerve cells in the heart have come in with the cardiac branches of the vagus nerve.

As already stated, Dogiel has found in the mammalian heart that the medullated fibres, which enter the heart, do not terminate around the nerve cells of one ganglionic group, but individual fibres can be traced to a considerable distance after they have made connexion with one group of nerve cells before they terminate in arborizations around a final group of cells; in their course they give off collaterals to other groups of cells. There is some evidence that these are true connector fibres, in that axon reflexes can take place through them; in the tortoise *Testudo græca* I found that one of the coronary veins frequently passed free from the rest of the heart between the ventricle and sinus, so that the auricles could be cut away from the ventricle and still leave the latter in connexion with the sinus by this vein. As a rule a small nerve, to which I gave the name 'coronary nerve' accompanies this vein. The fibres of this nerve are medullated and belong to the vagus (usually the right vagus). When the ventricle is thus isolated, I found that, with the electrodes placed on the ventricle itself or on this coronary nerve close to the ventricle, I could affect the rhythm of the sinus and the contractions of the auricles even when the current was so weak as not to cause any contraction of the ventricle. Such effect was always of an inhibitory nature, shown by slowing of rate and diminution in the force of the auricular contractions. This effect is most probably due to an axion reflex of the same nature as has already been described in the connector fibres of the sympathetic.

This same peculiarity of the tortoise heart enabled me to give evidence that the nerve fibres, which pass from these vagus cells

in the heart, are inhibitory in nature right up to their terminations in the muscular tissue itself. The auricle is separated from the sinus and left in connexion with the ventricle, the coronary nerve alone connecting the ventricle and auricle with the vagus nerve. The contractions of auricle and ventricle are registered separately. Such a preparation remains still for a long time and then contractions begin, which gradually and slowly increase in rate. If the right vagus in the neck is then stimulated no alteration of rate is caused, but a marked diminution in the strength of the auricular contractions is seen as the result of the stimulation. The fibres of the vagus then, which run in the coronary nerve, inhibit the contractions of the auricle. If the vagus is stimulated before the contractions begin, when the auricle is quiescent, there is no visible result, but the galvanometer shows that a change of potential takes place in the muscular tissue of the auricle of the opposite kind to what is seen when a contraction occurs, the muscle becomes more positive instead of more negative. These experiments have been confirmed recently by Meek and Eyster and Samojloff and are evidence that a chemical change is caused in the muscle by inhibitory nerve fibres producing a change of potential of an opposite kind to that produced by the action of a motor nerve.

I have considered the evidence for the existence and position of the various groups of inhibitory cells for unstriped muscle belonging to the skin, gut system, and heart, and propose to take now the evidence for inhibitory nerve cells and fibres for the unstriped muscles of the vascular system. It is at first sight strange to find that, although the existence of inhibitory nerve cells is as clear and undisputed in the case of the unstriped musculature already considered as the existence of motor nerve cells, there is no undisputed evidence for the existence of inhibitory nerve cells to the vascular unstriped musculature, although the existence of their motor cells is indisputable. There is a large amount of evidence to show that the blood vessels of an organ may dilate upon stimulation of an efferent nerve, especially if that nerve sets the organ at the same time into activity, and again and again the doubt arises whether the dilatation observed is really due to the action of vaso-dilator nerves, or is brought about in some way in consequence of the activity of the organ. We must always remember that the vascular system is to be regarded, not as a system

independent of the organs it supplies, but rather as a handmaid of such organs, supplying more or less blood to them as they require, and therefore that the regulation of the calibre of the blood vessels might be brought about otherwise than by the action of inhibitory nerve cells. At the present day it is recognized that the metabolism of an organ may be affected by the activity of another organ even at a distance, without the intervention of the nervous system, by means of chemical factors conveyed from the one organ to the other by the circulation; the classical example of such chemical messengers or hormones is the passage into the circulation of secretin from the duodenal mucous membrane to bring about the activity of the pancreatic gland. In any case of vascular dilatation we must always bear in mind the possibility of a direct chemical action upon the small blood vessels by the products of metabolism of the organ rather than an 'inhibition' by inhibitory nerves, and it is possible that the main factor in the regulation of the blood supply to an organ may be chemical rather than nervous.

But in addition to ensuring a greater supply of blood to an organ, when that organ is in activity, the vascular system requires regulation in its relation to the central organ, the heart, the efficiency of which is dependent so intimately upon the blood pressure in the vascular system; such a regulation is essentially of a nervous nature and makes it probable that the vascular muscles like the other muscles of the involuntary system possess inhibitory as well as motor nerves.

The first evidence for the existence of nerves which dilated blood vessels was given by Claude Bernard, who found that stimulation of the chorda tympani caused not only secretion of the submaxillary gland but also dilatation of its blood vessels. Then came the observation of Eckhard upon the meaning of erection, in which he showed that, when erection was caused by stimulation of the nervus erigens, there was a marked dilatation of the blood vessels of the penis. Vulpian showed the reddening of the tongue upon stimulation of the lingual nerve and proved that these dilator fibres came from the chorda tympani. Later Loeb and Eckhard showed that the tympanic branch of the glossopharyngeal behaves to the parotid gland and its blood vessels in the same manner as the chorda tympani to the submaxillary gland and its blood vessels. As early as 1869

Ludwig and his pupil Sadler were investigating the flow of blood through muscles in a condition of rest and activity. These investigations were continued by him with my assistance in 1874–75, and showed most clearly how great was the increase of flow through the muscle in consequence of the stimulation of its nerve.

About the same time Goltz had noticed that, whereas stimulation of the sciatic nerve when fresh cut caused a diminution of redness in the skin of the toes and a lowering of temperature as measured by a thermometer placed between the toes, the same stimulation of the nerve, if cut two days before, gave a reddening and an increase of temperature of the toes. He concluded that vaso-dilator as well as vaso-constrictor nerves existed in the sciatic and that they resisted degeneration for a longer time than the vaso-constrictors. These observations of Goltz gave rise to a number of other investigations made for the purpose of showing the existence of these vaso-dilator nerves in the fresh-cut sciatic. It was found by the method of rhythmical stimulation that the dilator nerves could be excited with stimuli which failed to excite the vaso-constrictors ; and further that reddening and rise of temperature in the foot could occur to a well-marked degree, if only the foot was cooled down sufficiently before the sciatic was stimulated (Bernstein).

Such were the main facts on which the existence of special vaso-dilator nerves was based.

The blood vessels alleged to be supplied by these vaso-dilator nerves are divisible into three groups :—(1) a group in which the vascular dilatation is clearly coincident with the activity of the organ ; this group includes all muscular and glandular organs ; (2) the blood vessels of the skin, especially investigated in the extremities, and (3) the blood vessels concerned with the production of erection of the penis.

I will consider first the increase in the flow of blood when a muscle contracts. My experiments in Ludwig's laboratory showed that the contraction of the muscle caused by direct compression an outspurt of blood at the commencement of the contraction ; this was followed by a diminished outflow during the muscular contraction and an enormous increase in the rate of flow immediately after the contraction. If the contraction lasted some time, the increase of flow might commence while the muscle

was still contracted. It seemed at first possible to attribute this great increase in the flow through the muscle to the mechanical effect on the blood vessels of the muscular contraction, for it was well known that if the rate of flow of blood through an organ is measured, and then for a time the blood is not allowed to flow through, upon the resumption of the circulation the rate of flow is seen to be markedly quicker than at the beginning of the experiment; an artificially produced condition of anæmia is always followed by hyperæmia of the organ. Such an explanation will not account for the great increase of flow when a muscle contracts; for, firstly, the contraction compresses the veins more than the arteries, and, secondly, I have found that a stimulus of the crural nerve lasting only four seconds causes a very much larger increase in the blood flow through the quadriceps extensor muscles than is produced by clamping the artery or vein to or from those muscles for as long as thirty minutes. There is certainly something more than can be explained by mechanical obstruction to the flow.

If curare be given in a sufficient dose, then there is no sign of either muscular contraction or increased flow upon stimulation of the crural nerve, although the increase of flow which follows upon section of the nerve due to the removal of vaso-constrictor influences is still manifested. If the curare was only just sufficient to prevent any visible contraction of the muscles, I found that stimulation of the nerve, especially by a series of cuts in it (crimping), was followed by a distinctly increased flow of blood through the muscles. This effect of curare pointed distinctly to a close connexion between the contraction of the muscle and the increase of the flow of blood through it, without the intervention of vaso-dilator nerves. On the other hand it was known that, although curare did not alter the activity of vaso-constrictor nerves, there was evidence that it prevented the activity of such nerves as the cardiac vagus, the nervus erigens, etc. On these grounds it seemed to me possible that the vascular dilatation was due to vaso-dilator nerves in the crural nerve, which was paralyzed by curare in a sufficient dose. On the other hand, it seemed to me that it was also possible to explain the increase of blood flow by the direct action of the muscular contraction, if the acid products produced by the contraction of the muscles were capable of relaxing the arterial muscular coat.

My observations upon the circulation through the mylohyoid muscle of the curarized frog, in which the muscle was spread out under a microscope and the size of the small arteries directly measured by a micrometer eyepiece, showed the dilatation of the arteries upon stimulation of the mylohyoid nerve even when there was not a trace of contraction of the mylohyoid muscle. This dilatation was not passive, caused by a possible stimulation of sensory nerves, for I observed simultaneously the circulation in the web and in the mylohyoid, and there was no constriction of the blood vessels in the web when the mylohyoid vessels dilated ; again, conversely, if on sensory stimulation the vessels of the web were made to constrict, no marked dilatation of the mylohyoid vessels was caused. These experiments thus pointed in favour of the vaso-dilator nerve hypothesis.

On the other hand I found that a very dilute solution of lactic acid (1 in 15,000 normal saline solution) caused a powerful dilatation of the blood vessels of the mylohyoid muscle, which was most striking and in marked contrast to the constricting action of a very weak alkaline solution. I concluded from this series of experiments, that it was perfectly possible for a muscle to increase automatically the amount of blood flowing through it when it contracted, because it would alter the chemical constitution of the lymph fluid in it, by the formation of acid metabolites ; and this more acid lymph on its way to the larger lymph vessels bathes and must affect the muscles of the fine blood vessels owing to the looseness of their adventitia. These experiments pointed directly to the activity of the muscle being itself the cause of the vascular dilatation without the intervention of special vaso-dilator nerves.

About the same time Severini put forward the view that the increased flow of blood through an organ, when it is in a condition of activity, is due to the trophic dilatation of the capillaries, and not to relaxation of the vascular muscles. He stated that oxygen diminishes the size of the capillary lumen, because the nucleus of the cells of the capillary wall (nucleus of Golubew) becomes more spherical, while conversely with the action of CO_2 it flattens out in the cell and so the lumen is greater. Apart from the fact that other observers have been unable to see any such alterations in the shape of the nucleus, my experiments on the vessels of the mylohyoid show clearly that the small arteries do dilate, and therefore any explanation of vascular dilatation

must account for such relaxation of the muscular coat of the small arteries. The difficulty of coming to any conclusion upon the cause of the dilatation of the blood vessels in muscles is due to the different effects of large doses of curare in the case of mammals and frogs; in the first case a large dose of curare will remove both the contraction of the muscle and the dilatation of its blood vessels upon stimulation of the nerve; in the second, however, even though much curare is given, the vessel may still dilate when the nerve is stimulated.

In one respect this dilatation in the mylohyoid is peculiar; it is always very temporary in nature, and in my paper I have given instances where, with a long stimulation of the nerve, the size of the artery measured increased to its maximum, and was back again to the size previous to the stimulation before the stimulation was finished. Also, without any stimulation at all, the calibre of the artery was varying in size considerably, thus producing, as shown in many of my figures, a series of irregular rhythmical dilatations.

Further, these assumed vaso-dilator fibres to muscle, are always found to be in the same course as the motor nerves to the muscle. Thus although section of the abdominal sympathetic will cause a great increase of flow of blood through the quadriceps extensor group of muscles, owing to the removal of tonic constrictor influences, the anterior nerve roots themselves must be stimulated to obtain the great increase of flow accompanying contraction of the muscle.

We come then to the conclusion that the increased flow of blood through muscle upon stimulation of the motor nerves to that muscle is chiefly due to the direct action upon the small blood vessels of acid metabolites formed by the activity of the muscle, but at the same time the presence of special vaso-dilator nerves is possible.

In close connexion with the regulation of the vascular supply to muscles is that to glands, and here again the evidence on the whole is in favour of a dilatation due to the metabolites of glandular activity rather than to special inhibitory nerve fibres. The problem is of much the same character as that already discussed in the case of muscle, the difference being that in this case it is the action of atropine instead of curare which has given rise to discussion. Keuchel observed that stimulation of the chorda tym-

pani no longer caused secretion in the submaxillary gland when atropine had been given, and Heidenhain pointed out that, even after atropine, stimulation of the nerve still caused an increased flow of blood through the gland; he therefore stated that fibres which caused the dilatation of the blood vessels existed in the chorda tympani independently of those which caused secretion; in other words, vaso-dilator nerves existed apart from glandular nerves. The same argument applies to other cases of glandular activity such as the parotid gland, noticed by Loeb and Eckhard, and the lingual glands. Severini has raised doubts of the validity of this reasoning, for he says that, even although atropine may prevent any external secretion through the ducts, it does not follow that it prevents all internal secretion into the blood and lymph fluids when the nerve is stimulated, and indeed he asserts that changes can be observed in the microscopic structure of the gland cells, even in the gland under atropine, when the chorda tympani is stimulated. Further these so-called vaso-dilator fibres, like the corresponding ones of muscle, are always in all parts of their course associated with the fibres which cause the activity of the organ.

Of recent years Barcroft has investigated the metabolism of the cells of the submaxillary gland under different conditions, by the estimation of the amount of oxygen taken in; and he has found that, coincident with the secretion of saliva and the increased blood flow through the gland, there may be as much as a sevenfold increase in the amount of oxygen taken up from the blood. He has also shown that this increased oxygen-uptake is not due to increased blood flow through the gland, for, if yohimbin be injected into the arterial supply to the gland, it causes no secretion of saliva and no measurable change in the oxygen used by the gland, although there may be as much as a tenfold increase in the blood flow through the gland. Also he has found that adrenaline, which like stimulation of the sympathetic will cause a secretion of saliva, causes also an increased flow of blood through the gland, which begins after the commencement of the flow of saliva, reaches its maximum after the salivary flow has reached its maximum, and persists after the flow of saliva has stopped, and long after the effect of the adrenaline has disappeared from the blood-pressure tracing. It causes also a considerable increase in the metabolism of the gland (in

one case fivefold) as judged by the intake of oxygen. He concludes from the extent of the metabolic activity that adrenaline causes a true secretion of the gland, which is accompanied by a marked increase of blood flow through the gland just as occurs when the chorda tympani is stimulated. Is this adrenaline dilatation to be ascribed to vaso-dilator nerves in the sympathetic, or to the action of metabolic products due to the activity of the gland?

Upon the injection of ergotoxine, Barcroft found that the subsequent injection of adrenaline causes no rise of blood pressure, no constriction of vessels in the gland, no secretion of saliva and also no increase of blood flow, showing that the increase of blood flow caused by the adrenaline cannot be ascribed to the stimulation of vaso-dilator nerves, but is due to the action of metabolites. After the ergotoxine, stimulation of the chorda tympani causes a flow of saliva and a dilatation of the blood vessels, as is to be expected from the nature of the action of ergotoxine.

It seems unlikely that, if the vascular dilatation due to adrenaline is not due to the stimulation of vaso-dilator fibres, the similar dilatation which occurs on stimulation of the chorda tympani should be due to such nerves. Barcroft has therefore investigated the evidence for metabolic activity in the gland when atropine is given and then the chorda tympani nerve stimulated. His researches are not yet published, but he allows me to state that the dilatation of the blood vessels on stimulation of the chorda tympani is less after atropine has been given than before, and further that the intake of oxygen is increased even though no secretion of saliva takes place. He considers then, in agreement with Severini, that some metabolic activity does take place in the gland even after atropine, and this in his opinion is sufficient to produce metabolites enough to account for the vascular dilatation observed, without the assumption of vaso-dilator nerves.

In the case of the blood vessels of all glandular tissues it cannot be said that the separate existence of vaso-dilator nerves is proved without doubt.

Let us consider now those blood vessels which supply epithelial surfaces. As already mentioned, it has been argued that, in a mixed nerve like the sciatic, the existence of vaso-dilator nerves, as well as of vaso-constrictors, is shown by the methods

of degeneration and of slow rhythmical stimulation. The vaso-dilators are held to resist degeneration longer than the vaso-constrictors, and can be excited by a weaker stimulus. In all the instances considered previously, namely of the vascular supply to muscles or glands, the marked characteristic has been that the so-called vaso-dilator nerves arise quite differently from the vaso-constrictor nerves, and have no connexion with the sympathetic system.

The evidence for vaso-dilator fibres in the sympathetic was given in the first instance by the observations of Dastre and Morat, which have been confirmed by Heidenhain and Langley. The former found that, while stimulation of the cervical sympathetic caused constriction of blood vessels over the head and face region, it caused at the same time a marked flushing inside the mouth and gums which was very visible in dogs and could be easily observed in white dogs; this bucco-facial dilatation was ascribed by them to the action of vaso-dilator nerves to these parts, which ran in the cervical sympathetic. No particular kind of stimulation was required and the phenomenon occurred with the freshly cut nerve. Neither Dastre, Morat, Heidenhain, or Langley have attempted to decide what part glandular secretion may play in this phenomenon. The places where the flushing has been observed are well supplied with glands, which are almost certainly supplied with secretory fibres from the cervical sympathetic. It is therefore more probable than not, that the flushing observed is explainable by the action of metabolites due to such secretion rather than as a result of stimulation of vaso-dilator nerves.

Secondly, the sympathetic may carry vaso-dilator nerves for the kidney. These nerves have been investigated by Bradford. He examined the roots of the thoracic and lumbar nerves, and found that stimulation of the posterior roots produced no effect on the kidney, but that constriction of its vessels with a rise of blood pressure was manifest on stimulation of the anterior nerve roots of the sixth thoracic to the first lumbar nerves in the dog (enumerating here seven lumbar nerves). The anterior roots of the eleventh, twelfth and thirteenth thoracic contained the main mass of renal vaso-constrictor nerves. He found further that when those same nerve roots were stimulated with a slow rhythmical stimulation (one shock per second), then instead of constriction a

decided dilatation of the kidney occurred without any rise of blood pressure and often without any appreciable fall. He concluded, therefore, that vaso-dilator nerves to the renal blood vessels exist and take the same paths as the vaso-constrictors.

Further, he found that stimulation of the peripheral end of the splanchnic nerve with the same slow rhythmical stimulation always caused a fall of blood pressure instead of the marked rise so well known upon ordinary faradic stimulation. This occurred quite markedly when the splanchnic nerve was stimulated above the entrance of the ramus communicans from the eleventh thoracic nerve, and as the presence of vaso-dilator nerves for the kidney could not be shown in the anterior roots of the sixth to tenth thoracic nerves, it is clear that this fall of blood pressure must be due to dilatation of blood vessels of the abdominal area other than those of the kidney. Bradford therefore concludes that the vascular area, supplied by the splanchnic nerve, receives both vaso-constrictor and vaso-dilator fibres, which pass out from the cord in the same anterior roots. These conclusions of Bradford have been confirmed by Dale, who has found that, after ergotoxine, stimulation of the anterior roots of the eleventh and twelfth thoracic nerves causes a dilatation of the renal vessels instead of a constriction ; and stimulation of the spanchnics causes a fall instead of a rise of blood pressure.

It is difficult to ascribe this vascular dilatation to the action of metabolites produced by the activity of the kidney, for there is no evidence for the existence of nerves which cause secretion in the kidney. At the same time there is some evidence that when the kidney is made to excrete by the presence of urea, its blood vessels are dilated. Roy showed that injection of urea into the blood caused not only a secretion of urine, but also a dilatation of the kidney vessels, even when all the nerves going to the kidney were cut. Seeing that urea injected into the blood flowing through an organ will not cause dilatation of the blood vessels of that organ, but does produce dilatation in the kidney vessels, it follows that such dilatation is a consequence of the activity of the kidney cells excited by the presence of urea, and can be explained in the same way as the dilatation which occurs in the submaxillary gland or in active muscle.

Finally, we come to the question of the causation of erection.

Eckhard, the discoverer of the *nervi erigentes*, has shown that erection is due to a relaxation of the muscular coats of the arterial blood vessels supplying the corpora cavernosa and spongiosa, in consequence of which the blood spurts out of the cut surface of the corpora cavernosa almost as forcibly as out of a cut small artery ; the flow through the dorsal vein of the penis is enormously increased, and the colour of the blood in it becomes arterial rather than venous. Here, then, there appears to be a vascular dilatation caused by nervous stimulation for a specific purpose, apart entirely from all connexion with any glandular or muscular metabolism. The nerve in question, the pelvic nerve, which causes this effect, belongs to the sacral outflow, and the only glandular secretion which is known to occur, when this nerve is stimulated, is that of the prostate gland. Barrington has, however, shown that this is not a true secretion, but is due to pressing out of a secretion owing to the contraction of some of the muscles surrounding the prostate gland. He has pointed out that a squeezing of the gland takes place both when the pelvic nerve and the hypogastric nerve are stimulated, from which he concludes that the muscle fibres round the gland are of two kinds, partly belonging, to use my nomenclature, to the cloacal muscles, partly to the urodermal group. He finds no evidence of true secretory fibres in the pelvic nerve, but marked evidence of their existence in the hypogastric nerve ; the evidence is also clear that the hypogastric supplies Cowper's glands and Bartolini's glands with secretory fibres. If then the metabolic products of the activity of any of these glands were concerned in the causation of erection, the *nervus erigens* ought to be found in the hypogastric not in the pelvic nerve.

At present I conclude that the phenomenon of erection can be best explained by the action of inhibitory nerves to the muscular walls of the arteries of the penis.

In the case of the bucco-facial dilatation, of the nervi erigentes, of the kidneys and of the muscles, the nerves which produce the vascular dilatation have been shown to leave the cord by the anterior roots, and it has been presumed also that the nerves in the sciatic, which on slow rhythmical stimulation cause a reddening and rise of temperature in the foot, are also anterior root nerves. Here, however, there arises a new and most unexpected factor in this question of the existence of vaso-dilator nerves, for

Stricker pointed out in 1876 that stimulation of the peripheral end of the posterior roots of the nerves, which help to form the sciatic nerve, cause a marked reddening and rise of temperature in the foot.

This was confirmed by Gärtner, and has been further investigated by Bayliss, who found, upon stimulation of the posterior roots of the fifth, sixth, and seventh lumbar nerves and of the first sacral nerve, not only a reddening of the skin and a rise of temperature in the toes, but also an increased volume of the lower limb, as shown by the plethysmographic method. No special method of stimulation was necessary, mechanical or electrical stimulation were both effective, pinching especially so. The fibres which produce the effect do not pass into the abdominal chain of the sympathetic, but go direct to the limb. Their trophic centres are in the posterior root ganglion, as is shown by the persistence of the effect after section of the posterior root between the ganglia and cord, and its removal after extirpation of the ganglion. Bayliss comes to the conclusion that this vascular dilatation is brought about by the stimulation of ordinary sensory nerve fibres acting anti-dromically. The blood vessels in question are not those which supply muscles, but are cutaneous vessels, for when the ankles and foot only are put into the plethysmograph the effect is very large, and when the skin is removed the effect is gone.

These observations make it still more difficult to come to any conclusion upon the nature of vaso-dilator nerves. It does not seem possible simply to substitute sensory nerves of the skin for vaso-dilator nerves in the explanation of the experiments of Goltz, Luchsinger, etc.; for not only do Bradford's experiments in the kidney show that the slow rhythmical stimulation of nerves, which are not sensory, will cause vascular dilatation, but Ellis has shown that the slow rhythmical stimulation of the sciatic in the frog causes dilatation in the web, while Oinuma working with Langley found no trace of either dilatation or constriction on stimulation of the posterior roots belonging to the sciatic.

Perhaps the safest way of looking at the matter in our present state of knowledge is to hold that vascular dilatation of an organ can take place in two ways, either by alterations in the chemical constitution of the fluids bathing the muscles of the small arteries, or by the stimulation of nerve fibres which relax those muscles;

at the same time recognizing that the existence of such nerve fibres is much less certainly proved than that of inhibitory nerve fibres to other involuntary muscles, such as the retractor penis and bladder musculature. With respect to the dilatation of blood vessels in the skin brought about by stimulation of the peripheral ends of sensory nerves I would suggest that an explanation may be found in the following arguments.

The condition of the epithelial cells of the skin is dependent on the integrity of the sensory nerves (glossy skin, etc.). Therefore the sensory nerves of the skin affect the metabolism of the cutaneous epithelial cells. When the chorda tympani, which is the secretory nerve to the submaxillary gland, is cut, a paralytic secretion of the gland takes place and the gland cells atrophy. When a sensory nerve is cut the epithelial cells atrophy and glossy skin results. The sensory nerve may be considered to control the metabolism of epithelial cells in a manner exactly comparable to the control of gland cells by their secretory nerve. Stimulation of the chorda tympani causes secretion, and that secretion is accompanied by dilatation of the blood vessels of the gland owing as suggested to the influence of acid metabolites upon the vascular muscles. If stimulation of a sensory nerve causes metabolic changes in the epithelial cells, corresponding to those in the submaxillary glandular cells upon stimulation of the chorda tympani, then the formation of acid metabolites would cause dilatation of the blood vessels of the skin just as in the case of the submaxillary blood vessels.

CHAPTER VII

THE INHIBITORY NERVES TO THE INVOLUNTARY MUSCLES OF THE EYE

THE last muscular group to be considered, with respect to this question of inhibitory fibres, is the prosomatic group of involuntary muscles, the motor cells of which are found in the ciliary ganglion. The movements of the pupil are regulated by two muscles of antagonistic action, the sphincter muscle and the dilator muscle. One would expect therefore to find, in accordance with the law of reciprocal innervation already given in so many instances, that the motor nerves to the sphincter muscle are accompanied by inhibitory nerves to the dilator muscle and vice versa. In other words, stimulation of the roots of the third nerve ought to cause relaxation of the dilator muscle, and stimulation of the cervical sympathetic ought to produce relaxation of the sphincter muscle.

There is a certain amount of evidence that such is the case. Weymouth Reid investigated the electrical changes in the two muscles, which occur on stimulation of the cervical sympathetic and roots of the third nerve respectively, by the same method as I had used in the case of the heart. The iris being exposed, he made a thermal injury across the sphincter muscle in one case, and across the radial muscle in the other, and obtained in each case a marked demarcation current when the electrodes were placed upon the injured and uninjured parts of the muscle. The first position of the electrodes he calls the concentric position, the second the radial. With the electrodes in the radial position stimulation of the cervical sympathetic gave a negative variation of the current indicative of a contraction of the dilator muscle, and in the concentric position a positive variation of the current indicative of a relaxation of the sphincter muscle. On the other hand stimulation of the roots of the third nerve gave the reverse effects, a negative variation in the concentric position, and a positive variation in the radial position. These experiments indicate that a true reciprocal innervation is present in this system also.

CHAPTER VIII

THE RHYTHMIC AND PERISTALTIC MOVEMENTS IN THE INVOLUNTARY MUSCLES OF THE VERTEBRATE

WE may profitably embody the arguments in the previous chapters in the following conception of the nature of the innervation of all involuntary muscle.

The motor nerve cells of all involuntary muscles (including in this term also those giving off inhibitory fibres) were originally, like those of voluntary muscles, situated within the central nervous system, and corresponded therefore to the anterior horn cells which send motor fibres directly to the voluntary muscles. They have left the central nervous system and formed the various groups of peripheral nerve cells, being still joined by connector fibres with connector cells in the central nervous system. These connector fibres form three main outflows, bulbar, thoracico-lumbar and sacral, known respectively as the vagus group of nerves, the white rami communicantes and the pelvic nerves.

Further the evidence shows that the afferent nerves belonging to the involuntary nervous system are in connexion with these motor nerve cells only by way of the central nervous system, for all the afferent nerve cells of the system are found in the posterior root ganglia, and none of them among the vagrant cells.

It looks as though the evolutionary process had acted in opposite directions in the case of afferent and efferent nerve cells of the involuntary system; causing in the former case a movement towards the central nervous system, in the latter, away from it.

This conception implies that there is no complete peripheral nervous system belonging to the involuntary muscles, but only motor neurons.

Another school of thought exists, which argues that a complete peripheral involuntary nervous system does exist and pervades all involuntary muscles; and is acted upon by regulating

fibres from the central nervous system. To this intrinsic nervous system all normal rhythmic action in these muscles is supposed to be due, and through the medium of its afferent and efferent nerve fibres co-ordinated movements are carried on, whether in the form of such peristaltic movements as those of the intestine or an orderly sequence of contractions as in the case of the heart. It is maintained that this intrinsic nervous system is composed of a network of fibres, with inclusive nerve cells situated within the organs themselves; and is therefore exclusive of the groups of nerve cells which lie outside the organs and can be removed without prevention of rhythmic or peristaltic action.

I will first take the question of rhythmical and peristaltic movements as shown in the case of the heart, and consider the evidence of the part played by the nerve cells in the heart itself.

Three possibilities suggest themselves:—

1. The nerve cells in the heart discharge rhythmically, and the heart muscle behaves in a manner similar to voluntary muscle and has no special rhythmic power.

2. The rhythmic power is in the cardiac muscle, and the nerve cells assist in the maintenance of that rhythmic power by maintaining the muscle in that fit condition of instability which results in rhythmic contractions.

3. The nerve cells within the heart have no more to do with the rhythmic power of the heart than the nerve cells outside the heart. In both cases they and their nerve fibres are regulators not initiators of rhythm; the rhythmic power is in the muscles themselves.

The history of the investigations upon the origin of the rhythm of the heart shows that, with the discovery of the ganglion cells in the sinus of the heart (Remak's ganglia), the rhythmic beat was naturally attributed to the action of those ganglion cells; and the conception arose that these cells were motor cells, which discharged rhythmically and sent separate impulses to the muscular tissue of the heart, thus causing separate contractions and bringing about the rhythmic beat. The due sequence of the contractions of the different chambers of the heart was brought about by a nervous mechanism, presumably ganglionic in nature, interposed between the main motor centres in the sinus (Remak's ganglia) and the auricular and ventricular muscle masses respectively. Nerve cells with such presumed nervous function were found by

Ludwig on the course of the nerve fibres running through the auricles in the case of the frog, and have been called Ludwig's ganglia, and others in the course of the nerve fibres to the ventricle at the auriculo-ventricular junction which have been called Bidder's ganglia.

These accessory groups of nerve cells do not initiate rhythmic impulses as long as the sinus ganglia are intact; if, however, the latter are removed, then these cells are capable of discharging rhythmic impulses in a similar manner to those of the sinus ganglia. The conceptions may be represented as follows:—

The rhythmic discharges from the motor centre in the sinus along the nerve fibres necessarily cause the sinus muscle to contract first, because they pass direct to that muscle; they cause the auricle to contract next, because of the delay of the impulse caused by the passage through Ludwig's centre, and finally the ventricle contracts last, owing to the further delay caused by the passage through Bidder's centre. If the sinus be removed then Ludwig's centre will become the motor centre, and still the ventricle will respond in due sequence to the auricle because still the impulse has to pass through Bidder's centre to get to the ventricle.

This view represents the neurogenic theory of the heart beat as it was developed in the first instance; it allows no rhythmic power in the cardiac muscle itself, which contracts simply to each rhythmic nervous discharge, just as though it were a piece of the muscle of the diaphragm responding to the discharges from the respiratory centre.

There is however abundant proof that all muscular tissue possesses to a greater or less degree the power of rhythmic response to an appropriate constant stimulus whether such stimulus be of a physical or chemical nature. Thus even ordinary striated muscle can be made to contract rhythmically by immersion in a suitable solution, and Mines gives instances of

the remarkable regularity of such rhythmic contractions of striated muscle. Undoubtedly some muscles are much more easily excited to rhythmic contraction than others; and I have put forward the view that the more primitive forms of muscle possess a greater rhythmic power than the more highly developed forms, in which rapidity of contraction has been gained at the expense of this rhythmic power.

In the case of the vertebrate heart, I have pointed out that it arose as a vascular tube surrounded by a layer of muscles. The tube became bulged in two places to form the large cavities of auricle and ventricle, and the musculature of these bulged portions contracted more rapidly so as to form a more and more efficient force pump. The more unmodified portions of the original tube are represented by the sinus, the canalis auricularis between auricles and ventricles, which ultimately becomes the junction between the auricles and ventricle at the auriculo-ventricular groove, and the muscles round the aorta which form the bulbus arteriosus in the frog and the conus arteriosus in the Elasmobranch fishes. Further the rhythmical power of the different parts of the heart was greatest in those parts where the original musculature had not been modified, i.e., sinus, auriculo-ventricular junction and conus arteriosus. Especially striking was the behaviour of the conus arteriosus of the Elasmobranch fishes, which, like the bulbus arteriosus of the frog, as pointed out by Engelmann, possesses a very high degree of rhythmic power.

This evidence combines to show that in any consideration of the meaning of the heart beat, both in warm- and cold-blooded animals, the rhythmic power of the muscular tissues must be taken into account.

With respect to the sequence of the contractions of different parts of the heart, my experiments on the tortoise showed not only that the sequence was not dependent upon the integrity of the main nerves, which pass from the sinus to the auricles and ventricles, but that a contraction wave travelled over the auricular tissue to the ventricle, and, when it reached the ventricle, the ventricular muscle contracted. Further, a block could be made in the series of contractions which reached the ventricle by reducing the size of and damaging the bridge of auricular tissue, over which the contraction wave had to pass; according to the amount of reduction and damage to the tissue at the bridge,

a delay in the passage of each contraction over it might occur just as ordinarily takes place at the auriculo-ventricular junction, or every second contraction might pass, or every third, fourth, etc., contractions. In all cases the ventricle remained quiescent until the auricular contraction reached it. These experiments convinced me that the beat of the heart was due to a peristaltic wave of contraction which started in the sinus and travelled over the muscular tissue of the auricles to the ventricle and bulbus arteriosus, the rate of travel being quicker in the bulged portion of the auricles and in the ventricle than in the more unaltered portions of the original muscular tube. Thus I came to the conclusion that the efficiency of the heart of the cold-blooded vertebrate as a force pump could be explained by the nature of the alteration of its muscular tissue in the course of development.

I pointed out at the same time that between the sinus and the ventricle on the dorsal side of the heart a flattened band of tissue existed from which on each side the reticulated structure of each auricle arose. This flattened band, which I called the junction wall between the auricles, and McWilliam called the sinus extension, has its muscles much more circularly arranged than in the bulged portion of the auricles. In this band the coronary vessels and large nerve trunks pass from ventricle to sinus; very frequently one of the coronary vessels passes free from the rest and with it runs one of the nerves passing along from sinus to ventricle. This nerve I called the coronary nerve, it is only one among many others which are present in this band of tissue. Experiment shows that its fibres belong to the right rather than to the left vagus.

With respect to the two parts of the auricles, namely this flattened band and the bulged portion, I pointed out that if the bulged part of the auricles was cut away, and this flattened band alone left, no contraction passed into the ventricle from the sinus, although all the nerves were in this band and the part in the auriculo-ventricular junction where they entered was richest in ganglion cells. On the other hand as long as the bulged portion of the auricle was left—even the very smallest piece—the contractions passed to the ventricle which responded to each one. I also examined the atrio-ventricular junction itself, and found that the ventral side close against the aorta was mainly responsible for the sequence of the contraction wave to the ventricle,

that the lateral part near this was partly responsible, and that the dorsal part, where the sinus extension joins the auriculo-ventricular junction, had no part in the passage of the contraction to the ventricle, for when alone left, no contraction of the ventricle took place. The small amount of tissue that could be left near the aorta without interrupting the sequence was amazing. The conclusion to which I came in 1888 was, that the muscular tissue, along which the contractile wave passed to the ventricular muscle, was especially situated at the ventral side near the aorta, and was in connexion with the reticulated muscular tissue of the auricles. At the same time I thought, as also did McWilliam, that the more circularly arranged tissue in the sinus extension might also, though at a slower rate, conduct a wave of contraction right into the ventricle.

Recently Laurens has taken up the re-examination of this question in the tortoise and lizard. What I have called the junction wall between the two auricles, and McWilliam the sinus extension, he calls the sino-ventricular ligament or dorsal ligament. He has repeated my experiments and found exactly the same results. He describes the auriculo-ventricular junction as shaped like a funnel and looks upon it, as I did, as the modification of the canalis auricularis. According to him there is no muscular continuity from auricle to ventricle on the dorsal side, but only on the ventral and lateral sides; here, strands of muscular tissue pass from the auricles directly into the ventricular muscular tissue. Külbs and Lange have demonstrated the same facts in amphibians, reptiles and birds, and in all cases have found that this connecting musculature is more embryonic in character than that of the auricles and ventricles.

What was true of the cold-blooded heart I felt sure was true of the warm-blooded, and I was much pleased when Stanley Kent undertook to investigate the nature of the passage of the contraction wave from auricle to ventricle in the mammalian heart. He demonstrated that strands of muscular tissue did connect auricle and ventricle together. His investigations were confirmed later by His junior, after whom these bundles of muscle fibres are known in Germany, being called the bundle of His. The most important investigation of the nature of this connexion was made later in Aschoff's laboratory by Tawara, who showed that the connecting strands were composed of a peculiar primitive

kind of muscle fibre known as Purkinje's fibres. He described how these peculiar large fibres passed into the ordinary muscle fibres of the ventricle on the one side, and formed a tangled knot of peculiar small fibres on the auricular side, the contingents of which passed into separate auricular muscles. This knot is known by the name of the auriculo-ventricular node.

A similar structure has been described at the junction of the veins and the auricles, "the sino-auricular node" of Keith and Flack, from which the beats of the heart start. This sino-auricular node has been further investigated by Lewis; it is a structure of the same kind as the auriculo-ventricular node, and forms an elongated mass in the sulcus terminalis at the junction of the right auricle and vena cava superior. Here the reticulated muscle strands of the auricles come together to form a muscular band known as the tænia terminalis, from which muscle fibres pass into the vena cava superior and inferior. The peculiar fibres which form the sino-auricular node are of the same kind as those in the auriculo-ventricular node, "being small, about a half or third the breadth of those of auricular fibres proper" (Lewis, p. 2).

The theory that I put forward to explain the peculiarities of the heart beat in the cold-blooded vertebrates, has thus received striking confirmation in the investigations on the heart of warm-blooded animals, and has been confirmed by recent investigation on cold-blooded animals; in all cases the parts of the heart, where rhythmic beats may start, and where the conduction of a contraction wave is slower, consist of muscular tissue of a more primitive type, the remains of the canalis auricularis and of the sinus venosus.

This then represents what has been called the myogenic theory of the heart beat, in which the initiation of a rhythmic beat and of the maintenance of a due sequence of contraction from cavity to cavity are ascribed to the muscular rather than to the nervous elements in the heart. At the same time this theory does not imply, and has never been intended by me to imply, that the nervous tissues in the heart have nothing to do with the heart beat. I have always been a strong believer in the close connexion between the muscle cell and its nerve and nerve cell, and consider that there is abundant evidence to show that the well-being of the muscle is dependent upon the integrity of its connexion with its nerve cell; with the

removal of the nerve-cell the condition of the muscle is profoundly altered; and it is, in my opinion, highly probable that the normal beat of the heart is dependent on the muscular tissue, where the beat originates, being kept in the due condition for spontaneous contractions by the action of nerve cells in the heart. The whole object of my researches on the rhythm of the heart was to answer the two questions: "Do motor nerve cells in the heart send out rhythmic impulses to the muscular structures of the heart?" and "Is the sequence of the contractions of the different heart cavities due to impulses passing along the main intra-cardiac nerves, which reach the muscular structures of the separate cavities in orderly sequence?" These two questions I claim to have answered definitely in the negative.

The observations of Carlson on the rhythm of the heart of Limulus have served to resuscitate the neurogenic theory of the heart's action. In this animal the cardiac nerve cells are grouped together into a cord, which lies on the surface of the heart and can be easily removed without damaging the muscular tissue in any way. It is found that after removal of this nerve cord the heart entirely ceases to beat. Carlson, therefore, argues that the rhythm of the heart is entirely dependent on the presence of the nerve cells in this cord and is in no way a function of the muscular tissue. He implies that motor nerve cells in the cord discharge rhythmic impulses along the nerves in the heart, and that the heart muscle contracts to each impulse; in fact, that the motor nerves to the heart muscle resemble the phrenic nerves to the diaphragm in the part played by them in the rhythmic contraction of the muscle. Carlson has not, however, yet completed the resemblance, for he has not been able to show by means of the galvanometer that rhythmic discharges do pass along these cardiac nerves when the heart is beating, as can be shown in the phrenic nerve in the case of the respiratory discharges. Further, and this seems to me a very important consideration, Carlson states that the removal of the nerve cord leaves the muscular tissue in a condition of inhibition similar to that caused by stimulation of the inhibitory nerves, from which he argues that the inhibitory nerves act by removal of the impulses from the motor nerve cells and not by direct action on the muscular tissue; but it also shows that the condition of the cardiac musculature is profoundly altered by removal of the

nerve cells, with which it is in connexion. As long as the muscle remains in that condition it could not be expected to exhibit any rhythmic power, even if it possessed such power in a marked degree. Carlson himself has shown that such is the case, for, in the heart deprived of its nerve cord, a rhythm, sometimes very regular, can be induced by plunging the heart into a solution of sodium chloride. The manner in which the salt solution brings about this myogenic rhythm is very suggestive, for Carlson states that first the excitability improves so that each stimulus causes a better contraction, then instead of a single contraction a single stimulus will cause a number of contractions, and finally with the increasing number a stage is reached where a stimulus is unnecessary and spontaneous beats take place. The whole phenomenon is reminiscent of the stages passed through by the strip of the auricular muscle of the tortoise on its way to spontaneous contraction.

It seems to me that Carlson's observations of the rhythm of the heart of Limulus are in strict accord with the rhythmic phenomena exhibited by the vertebrate heart, if we assume that in each case the nerve cell does not send out rhythmic discharges to the muscle, but keeps the muscle in such a condition of tension that it can contract rhythmically. The intrinsic nerve cell behaves to the muscle of the heart in the same manner as the extrinsic nerve cell of the sympathetic ganglion behaves to the muscle of the artery, the difference in result being due to the physiological difference between the two muscles, thus causing in the one case rhythmic contractions, in the other tone.

The observations which have been made on the lymph hearts of the frog are very instructive in connexion with this question. The ordinary rhythm is undoubtedly neurogenic in the sense that it is dependent on the central nervous system. The nerves to the lymph hearts are motor nerves, and their stimulation causes tetanus of the striated muscle of the heart; again, as in skeletal muscle or in the Limulus heart muscle, the strength of contraction depends on the strength of stimulus: the "all or none" principle does not apply. The excised heart remains motionless in winter but in summer irregular spontaneous beats occur. A weak tetanizing current sent through the excised heart causes a more or less rhythmical activity during the stimulation. From these observations it is clear that the musculature of the lymph

heart resembles closely the musculature of the Limulus heart. In both cases the musculature possesses rhythmic power, but the normal beat does not occur when the muscle is first separated from the motor nerve cells. When started it may, however, persist for a long time, for Stefanowska found it beating six to eight days after destruction of the spinal cord. Finally Tschermak has shown that these cells in the case of the lymph heart maintain a tonic not a rhythmic influence on its musculature, for there is no sign of any periodic movements in a delicate capillary electrometer when it is connected with the central end of the nervus coccygeus superior.

So far the evidence appears to me to show that the nerve cells within an organ such as the heart (the intrinsic cells) cannot be looked upon as different in character from those not imbedded in the organ (the extrinsic cells).

Following the heart come the blood vessels, in which well-defined nerve cells are few and far between : that such do occur is clear from Jegorow's picture, fig. 8. He describes also by the methylene blue method a network of nerve fibres closely surrounding the muscular coat of the blood vessels, but does not figure nerve cells in this network. Langley has shown that this network entirely degenerates when the motor nerves to muscles of the blood vessels have been cut. In the meshes of the network nodal thickenings have been described and have been called nerve cells ; but they are unable to keep alive the network after the separation of the extrinsic motor nerves.

The same also holds in the allied case of the dermal system of involuntary muscles. We may take as an example of these muscles the Retractor penis, as that muscle has been more carefully examined than any other. Its motor fibres arise from cells in ganglia of the lumbar chain, and its inhibitory fibres from cells in the pelvic ganglia : both these sets of ganglia are extrinsic, lying outside the muscle. In the muscle itself Fletcher finds a well-marked nervous network surrounding the muscle fibres. In this network there are no nerve cells, and when both the nerves are cut this network disappears : there are no intrinsic nerve cells to keep it alive. In all probability the same is true of the whole of the dermal musculature.

The most striking case of a regular normal rhythm in an artery is to be seen in the arteries of the leech. My son, J. F.

Gaskell, has made a special study of this rhythmic vascular system. In the leech there are two main longitudinal contractile vessels situated absolutely laterally, which function as hearts; from these cross vessels arise in each segment which in addition to supplying the body with blood connect the two lateral vessels together. These connecting vessels, like the two lateral vessels, are strongly contractile and like them are capable of independent rhythmical contractions. Now the nerve cells in the leech are very conspicuous and easily found wherever they are present. My son has traced the nerve fibres from the central nervous system to these blood vessels and never found a sign of a nerve cell between them and the muscles of the blood vessels. Also the regular rhythm of these lateral hearts continues after destruction of the central nervous system. The evidence seems to me quite clear that the muscles of the vascular system in the leech possess a normal rhythmical power entirely independent of the presence of nerve cells.

Finally we come to the consideration of the movements of the alimentary canal. According to the investigations of Kronecker and Meltzer the peristaltic wave of contraction, which passes along the œsophagus in the act of deglutition, is of such a character that a bolus in the œsophagus causes contraction of the œsophageal muscle just above it, and relaxation of the parts below. They attributed this law of peristalsis to the action of the central nervous system chiefly because of Mosso's observation that a peristaltic wave could be started at the upper end of the œsophagus and travel to the stomach, even when the œsophagus was completely cut through in its middle portion.

Later Bayliss and Starling investigated the problem in the intestine, and showed by means of the enterograph that here also, when a peristaltic contraction was caused by stimulation at a spot, the contraction commenced above the spot stimulated and was accompanied by a relaxation of the intestine below the spot. Further they showed that this 'law of the intestine' held good when all the nerves to the gut from the central nervous system had been cut; that, in fact, the mechanism, by which this co-ordinated peristalsis was brought about, existed in the intestine itself. They considered it to be nervous in nature, and that it was in all probability situated in Auerbach's plexus. It has been called the enteric nervous system.

Later Magnus carried out a number of experiments on an isolated piece of intestine suspended in Ringer's solution, and showed that if a separation was made between the two layers of muscle (longitudinal and circular) by means of a needle, so that the slit-up piece of intestine was divided into two parts, one containing the circular muscular layer, and the other the longitudinal muscles, then spontaneous movements occurred only in the latter half, while the circular musculature remained absolutely quiescent and upon stimulation gave a local contraction at the place of stimulation but no sign of any contraction wave. Upon microscopic examination he found that the whole of Auerbach's plexus was contained in the half containing the longitudinal muscles. He agreed therefore with Bayliss and Starling that Auerbach's plexus functioned as a central nervous system, in that impulses reached it from the stimulated point and produced effects of opposite character, namely excitation of motor cells in the parts just above the stimulus, and inhibition of those just below. Meissner's plexus he found, took no part in the manifestation of this reflex. This reflex has received the name of the myenteric reflex (Cannon).

This evidence appears to differentiate the enteric nervous system from the peripheral ganglia so characteristic of the sympathetic nervous system, which, as already argued, represent motor and inhibitory nerve cells of the involuntary nervous system, which were once situated in the central nervous system.

The evidence here seems rather to point to a complete peripheral nervous system with a reflex mechanism of a definite character, for the purpose of bringing about a necessary co-ordinated movement for the onward propulsion of the food; and supports therefore the view of those who, like Bethe and Nicolai, consider that in all organs containing unstriped muscle fibres a network of nerve cells and nerve fibres is found in close connexion with the muscles. This network represents, according to them, the original diffuse nervous system, spread over all contractile tissues, such as is seen in the swimming bell of the Medusa, out of which in the course of evolution a concentrated nervous system has arisen, except in the case of peripheral organs which contain unstriped muscle, where this original system still remains intact.

The other view, to which I incline, is that there is no difference between intrinsic or extrinsic nerve cells: both are motor or

inhibitory cells of the involuntary nervous system which have travelled out from the central nervous system to reach their destination. Certainly, as far as the sympathetic is concerned, the cells were originally in the central nervous system, and all the cases of reflex action described in this system have been shown by Langley and Anderson to be of the nature of axon reflexes. It does not however follow that the cranial and sacral outflows have been formed in precisely the same way as the sympathetic. Their cells tend to be scattered in the meshes of a nerve plexus rather than grouped in definite ganglia, as in the latter case, and their systems behave quite differently to adrenaline.

In Chapter I, I have taken it for granted that the motor cells connected with the connector nerve fibres of the vagus and pelvic nerves have travelled out from the central nervous system similarly to the sympathetic cells. The evidence given by Onodi was purely morphological, and had nothing to do with the function of the cells. According to this author a mass of cells exists in close contiguity to the cells of the posterior root ganglion throughout the spinal cord, which ultimately separate out and become peripheral. There is no reason to suppose that the same procedure does not take place in the sacral region, and thus form the peripheral cells belonging to the pelvic nerve, but as far as I know this has not as yet been shown to be the case.

There is a considerable amount of evidence that the nerve cells of the vagus system found in the heart and alimentary canal were originally in the central nervous system, and have travelled out to reach their destination. In the first place His junior has shown that the cells of the heart at first are not in the heart but in the course of development "travel" into it; he looks upon them as including sympathetic cells as well as vagus cells, and his evidence has been largely accepted as proof that these cardiac cells were originally situated more centrally, and have travelled farther away from the central nervous system during development. The evidence given by Kuntz and by Miss Abel both confirm the observations of His junior with respect to the travelling of the vagus nerve cells into the heart, and both deny any evidence of any such inclusion of nerve cells from the sympathetic system. Further, Miss Abel states that the vagal wandering cells are seen at first close against the root ganglion of the nerve, from

whence they can be traced to the heart and the intestine, and both she and Kuntz state that all the cells which enter into the intestine belong to this vagal system, and none reach it from the sympathetic system; that is to say, the cells of Auerbach's plexus are all vagal cells. The embryological evidence thus confirms the physiological, for the injection of nicotine, which prevents the action of the vagus nerves, both in the heart and in the gut, but does not prevent the action of the sympathetic nerves in either case, is proof that vagal cells alone exist in both the heart and the gut.

There is to my mind a difficulty in accepting the evidence given by both Kuntz and His as a complete proof of the wandering out of vagus motor cells to the periphery, for in both cases free nerve cells in the shape of neuroblasts are said to move independently peripheral-wards and afterwards to become connected with the central nervous system and to send fibres to the muscles and gland cells. Such a conception seems to me so highly improbable as to throw some doubt on the soundness of the observations. Still if we take simply the observations of these authors and leave out of account their statement that the cells in question are free wandering neuroblasts, it could then be said that the relative positions of these vagus nerve cells with respect to the central nervous system on the one side, and the peripheral organ on the other, does vary in the course of development in the direction of a more and more peripheral situation.

The evidence already given leads to the conclusion that the nerve fibres, which arise from the motor or inhibitory cells of the involuntary nervous system, terminate directly in their corresponding musculature, possibly by means of a fine plexus or network of nerve fibres immediately embracing those muscles, and do not terminate in any other nerve cells before reaching the muscle. From this it follows that in such cases as the heart and small intestine, where the inhibitory cells belong to the sympathetic system, and are situated outside the organ, there are no cells belonging to that system situated in the organ, and therefore that all nerve cells found in the heart or small intestine belong to the vagus system.

Those observers who look upon both heart and intestine as possessing an intrinsic nervous system complete in itself, and independent of the central nervous system, consider that this

system is connected to the central nervous system by nerve fibres from two sources belonging to the vagus and sympathetic systems respectively, each of which influences the nerve cell apparatus in the organs themselves. They do not it seems to me lay any importance on the difference of these two connexions; the nerve fibres of the one being pre-ganglionic or connector fibres with a medullated sheath and of the other post-ganglionic and usually non-medullated fibres. They see no difficulty in the view that the non-medullated accelerator and augmentor fibres of the heart or the non-medullated inhibitory fibres of the intestinal muscles should make connexions with another group of sympathetic cells within the heart and intestine respectively before reaching the muscular tissue.

The chief exponent of this view is Dogiel, and it is based mainly on histological evidence obtained largely by the appearances after staining the living tissue with methylene blue. In the case of the intrinsic nervous apparatus of the intestine of mammals, Dogiel finds in Auerbach's plexus two main types of nerve cells, which he designates as cells of Type I and Type II respectively. He speaks throughout of the cells of Type I as motor cells of the sympathetic system. Dogiel gives a history of the investigation upon the nature of Auerbach's plexus before his own, and points out that Ramon y Cajal in 1893 investigated Auerbach's plexus by his modified Golgi method, and came to the conclusion that the cells of the ganglia are multipolar and possess three to eight processes, which can be followed for a long distance. He considers these processes to be nervous and to form complicated plexuses round the muscular and glandular structures. The fibres which simply pass through the ganglia he considers to be non-medullated and to arise probably from sympathetic ganglia outside the intestine. In addition there are fibres which form arborizations round the cells, but he does not know where they come from. After Dogiel had described his two types of cells, la Villa, a student of Cajal, re-investigated and found Dogiel's Type I which had been missed by Cajal, because it was so much more difficult to stain than Type II. Cajal's description therefore refers to Type II exclusively.

In the course of the investigations into the structure of Ammocœtes, which Miss Alcock has carried on through so many years, she has found in the intestine groups of nerve cells of an

ordinary description, perfectly visible without any special staining method, in as close connexion with the fibres of the vagus nerve as are the cells of Remak's, Ludwig's and Bidder's ganglia in the case of the frog's heart. Manifestly such cells are the motor cells of the vagus system. In the case of this low form of fish, they are the only manifest cells to be found. Recently Sakuseff has investigated at Dogiel's suggestion the nature of Auerbach's plexus in the Teleosteans, Chondropterygians and Cyclostomes, by the methods of Golgi and Ehrlich, and has found in the two former classes of fish the two types of cells described by Dogiel, but in the cyclostomes only one kind of nerve cell, which belong to Dogiel's Type II.

Further Dogiel has traced from the cerebro-spinal or vagus nerves fibres which terminate by arborizations round nerve cells, and he finds such fibres traverse many ganglia and give off collaterals to their cells ; he does not state the type of cell around which they arborize, because, as a rule, when the staining allows cerebro-spinal nerve fibres to be traced a long way, the cells are not stained, but, judging from the evidence of the cyclostomes, they must be cells of Type II. Finally the body of the cell of Type II is round, rather than angular, and its processes of clean unbranched nerve fibres pass away from the ganglia along the bundles of nerve fibres which form the plexus, to end, according to Cajal, around the muscular or glandular cells.

Fixing then our attention on Type II alone, we see that in every respect the innervation of the gut is of the same character as that of other organs innervated by the involuntary nervous system ; the vagus fibres are connector fibres which, as in other cases, connect with many cells by means of collaterals, and these cells are the motor cells to that part of the gut musculature which belongs to the vagus system. There is no question of the sympathetic fibres connecting with such cells ; they pass through the ganglia, as described by Cajal, and do not connect with any nerve cells but go direct to muscles.

In another respect these motor cells in the alimentary canal resemble other motor cells of the involuntary system. The tone of the muscle normally depends upon them. Cannon has shown that in the stomach a tonically contracted band is seen at the incisura cardiaca during digestion, from which rhythmical contractions start and travel along the antrum to the pyloric end.

These rhythmical contractions depend upon a certain condition of tone in the muscle in combination with a stretching of the muscle due to the presence of food, just as is seen in other rhythmic organs such as the heart, where the stretching of a muscle possessing tone causes rhythmic contractions. If the muscle of the stomach is flabby and without tone, the rhythmic contractions cannot take place, even if its walls are stretched. Stimulation of the vagus nerve causes a tonic condition of the muscle, and then the rhythmic contractions take place upon distension. These rhythmic contractions are not confined to their place of origin but travel as waves of peristalsis, because each contraction causes a distension of the adjacent muscle, which although not in so extreme a condition of tone as at the band, is still in a condition of tone sufficient to react when distended. This travelling of a peristaltic wave is not dependent upon the integrity of either the nervous or muscular coats in the intestine, for Cannon has shown that, after one or more circular incisions round the stomach down to the submucous layer, after the animal has recovered from the operation, the peristaltic wave travels as easily as before the operation. It is not due therefore to any reflex nervous action through Auerbach's plexus but to the consecutive stretching of the walls of the antrum, the muscles of which are in a condition of tone.

There is another normal peristaltic movement of a similar character described by Elliott and Barclay-Smith in the large intestine, where the contents undergo a churning and squeezing action somewhat similar to what occurs in the antrum of the stomach. Here also a tonic band of constriction is seen to be formed always at the anal end of the proximal portion of the colon at a varying distance from the anus, from which rhythmic contractions arise and give origin to a series of peristaltic waves which travel in the direction of the cæcum. These anti-peristaltic waves depend upon a condition of tone, and are due to the distension of the tonically contracted muscle just as in the stomach. These two normally occurring peristaltic waves are dependent upon the nervous system of Auerbach's plexus only in so far as the nerve cells keep the muscle in a condition of tone. In neither case are they abolished by nicotine, and in neither case is the peristaltic or anti-peristaltic wave preceded by a wave of inhibition.

The ordinary peristaltic movements, in both small and large intestine, are looked upon as due to a different cause from the movements just considered, because they are preceded by inhibition and are put out of play by nicotine. Do such differences necessarily imply the presence of a true reflex nervous system in the intestine?

I do not think that our present knowledge enables us to speak positively on the subject. The main argument appears to be based upon the evidence of a co-ordinated nervous activity in the intestine, which shows itself by a purposeful inhibition of a part of the intestine towards which the peristaltic wave is travelling. This inhibition and the peristaltic contraction are both caused by the presence of a bolus in the intestine or a pinch at any spot, and are supposed to imply a true reflex activity in the myenteric plexus.

Now Bayliss and Starling, who discovered this law of the intestine, showed in the same paper that the peristaltic wave was not necessarily accompanied by a preceding relaxation of the intestinal wall, for upon repetition of the experiment many times in the same piece of gut, a most striking difference takes place in this so-called reflex, in that the insertion of the bolus still causes a contraction above the bolus but without any preceding inhibition below the bolus. This contraction passes as a wave of contraction down the intestine over the bolus without moving it onwards appreciably, looking as though a strong movement of the bolus was necessary for the causation of a preceding inhibition. So also, as pointed out by Cannon, a stimulation of the gut may cause inhibition above and not below the point stimulated. This has been observed by Bayliss and Starling, and by Magnus in the isolated intestine. These observations suggest that the inhibitory effect of a stimulus or a bolus is not necessarily closely bound up in a purposeful manner with a downward travelling peristaltic wave. It is possible to look upon the effects produced as due to the stimulus affecting two separate nervous arrangements, not necessarily closely bound up together; by the stimulation of the one, a peristaltic wave of contraction is caused, by the stimulation of the other, inhibition of some part of the gut is caused according to the arrangement of the inhibitory nerves at the place stimulated. It is striking, as Cannon observes, to see how variable is the

distance to which the inhibition extends after a single pinch of the intestine.

The known nervous factors in the small intestine which might react to a stimulus are :—

1. The inhibitory fibres which enter in with the branches of the superior mesenteric artery and arise from nerve cells in the superior mesenteric ganglion, whose connector fibres are in the splanchnic nerve.

2. The connector fibres of the vagus nerve, which connect with the motor nerve cells in the intestine, and by means of collaterals can affect a considerable area of intestinal muscle.

3. The motor cells themselves and their motor fibres to the musculature.

If the stimulus which brings about the so-called myenteric reflex affected at the same time 1 and 2, then the phenomenon observed would be accounted for without invoking any reflex and without the necessity of the supposition of a special enteric nervous system differing in principle from that of the sympathetic nervous system. The fact that the myenteric reflex does not necessarily require a strong stimulus for its manifestation, but can be produced by the presence of a bolus such as cotton wool and vaseline, is not a fatal objection to this hypothesis, for it is well known that distension of the lungs is alone sufficient to stimulate vagus fibres from the lung alveoli to the respiratory centre, so that local distension alone of the intestine may stimulate fibres of the vagus and splanchnics in the same way.

With respect to 1, Langley and Magnus investigated the question whether the inhibitory fibres from the cells of the superior mesenteric ganglion take any part in this so-called myenteric reflex, and they found that after removal of all the cells of the solar ganglion and as far as possible removal of the mesenteric nerves, and after a length of time sufficient for degeneration of all peripheral nerve fibres, the myenteric reflex was still demonstrable in the intestine. Evidently then, the reflex has nothing to do with the sympathetic nerve fibres in the gut. The phenomenon in question is therefore dependent solely on its vagus system.

In the case of the large intestine it would appear from the work of Elliott and Barclay-Smith that the hardness of the bolus plays an important part in bringing about the so-called myenteric

reflex, for they state that as long as the contents of the proximal colon are soft, a series of anti-peristaltic waves pass along it, which are not preceded by inhibition; as soon however as a portion becomes hard a normal peristaltic wave occurs preceded by inhibition and the hardened bolus is passed on to the distal part of the colon. A true reflex necessitates at least sensory and motor neurons in the intestine itself. At present we have no evidence of the existence of sensory nerve cells in the gut, while there is evidence that the sensory nerves of the gut arise from cells in the posterior root ganglia. The very fact that nicotine will prevent this reflex in the isolated gut, indicates that it is dependent on the integrity of the synapse between a nerve fibre and a nerve cell. The only nerve cells in the gut which are known to have such a connexion are the vagus nerve cells, so that the action of nicotine points in the direction that the reflex is due to a direct stimulation of vagus fibres, i.e., of connector nerves to the motor ganglia in the intestine. If, after the vagus nerves have been cut and time allowed for degeneration, the myenteric reflex becomes abolished, as the action of nicotine indicates, then it seems to me we should have proof positive that this so-called reflex is due simply to stimulation of vagus fibres in the intestine.

Although the investigation of the so-called myenteric reflex after complete degeneration of all the vagal fibres to the small intestine has not, as far as I know, been carried out, the corresponding experiment for the large intestine is described in the paper by Elliott and Barclay-Smith. The animal was a rat, and the cord was completely destroyed below the ninth thoracic segment; the muscles around the anal and vaginal orifices quickly regained a high tone, and at the end of the sixth week after the operation the colon was examined: "the disposition of the contents was abnormal and suggestive of a sluggish intestine. Though the rat had not been fed for the last twenty-four hours, its cæcum was full with material that extended into the lowest three inches of the ileum, through the relaxed ileo-colic sphincter. A large soft mass occupied the proximal colon, where such would assuredly never have been found in a normal animal: and the hardening nodules in the distal colon were irregularly piled on the top of one another. At no time were any movements seen in the intermediate and distal colon. Antiperistalsis was once

noticed in the proximal colon. The cæcum was the only decidedly active part, yet even its activity was weak. Not once was it seized by the deep blanching constrictions that occur in the normal animal. Those seen were of slow and oscillatory development, of shallow and irregular extent. The distal colon had lost its pre-ganglionic (connector) constrictor fibres : the whole its pre-ganglionic inhibitory and central sensory nerves. The ganglia of the autonomic visceral nerves, and those of the plexuses in the intestinal wall remained. They would not atrophy, and indeed their activity might have been expected to be the greater. Yet the movements observed—under light ether anæsthesia—were utterly inco-ordinated and very weak." I conclude from these observations of Elliott and Barclay-Smith that the co-ordination of movement, upon which the existence of a myenteric reflex is based, is gone when the connector nerves to the part have degenerated.

My views on the nature of rhythm in involuntary muscle may be summed up as follows :—

Involuntary muscle is covered over with a network of fibres, which arise from peripheral nerve cells. This network degenerates when separated from its parent nerve cells. The nerve cells belong to two nervous systems, the sympathetic and enteral systems, and are called intrinsic or extrinsic according to their situation upon the muscular organ or at a distance from it. The intrinsic cells have been considered to be of a different character to the extrinsic, and the initiation of rhythm in the involuntary muscle has been ascribed to the intrinsic only. It was manifestly impossible to ascribe it also to the extrinsic cells, for, being situated outside the rhythmical organ, they could be removed, and yet the rhythm continued. The intrinsic cells to which the rhythm is attributed, sometimes belong to the sympathetic system, as in the ureter, sometimes to the enteral system, as in the intestine and heart, sometimes they are inhibitory cells, sometimes motor.

The evidence is strong, that isolated pieces of muscular tissue will contract rhythmically in the absence of all nerve cells. Such pieces of isolated muscles always possess a nervous network round their muscle fibres, so that if the rhythm of the involuntary muscle is always to be regarded as of nervous origin, the initiation of rhythmic discharges must in this case be attributed to this

network. This is a proposition which is to my mind highly unlikely. All muscular tissue possesses the power of rhythmic contraction to a greater or less degree. Ordinary striated muscle, with its more rapid contraction, has lost this power to a much larger extent than unstriped or cardiac muscles. The more embryonic the muscle the greater is its rhythmic power.

The power of manifesting rhythm depends upon the condition of the muscle, upon what is often called a condition of tone; this condition does not necessarily imply contraction but rather a readiness to contract, owing to the muscle having attained a condition of unstable equilibrium. This condition of tone is dependent upon both nervous and chemical factors. As long as the muscle is in continuity with the nerve cell, which nourishes its nerve, the action of that nerve cell keeps the muscle in a condition of tone, so that it can manifest rhythmic contractions. When it is separated from its nerve cell it loses its tone, but that condition can be restored by the action on the muscle of certain chemical substances, especially salts of sodium, so that the rhythmic activity again becomes evident. This seems to me yet another instance of the condition of a tissue not being dependent solely on its connexion with the nervous system, but also upon chemical substances brought to it in its nutrient fluid. The nervous action upon which the tone of the muscle depends is ultimately conveyed to the muscle by the network of fibres on it. It is said to be a true network, not an interlacing of fibres, and in many cases it is formed from the axons of both sympathetic and enteral nerve cells. According to Fletcher's observations on the retractor penis muscle, it will not degenerate until separated from both systems of nerve cells.

It is, however, universally accepted that the separation of either nerve cell profoundly modifies any rhythmic activity present at the moment of separation, though later a readjustment may take place with the return to a condition very near or identical with the original; the permanent removal of the cells of one of the two systems, which are in connexion with the network, need not necessarily prevent an effectual control of tone by the peripheral network; that is to say, the integrity on the nervous side of one system only is sufficient to maintain a nervous control of tone. Thus the tone of the heart can be maintained by the intrinsic nerve cells alone, although they belong entirely to

the vagus system only. It does not follow that the maintenance of rhythm in an isolated heart implies that this rhythm is dependent entirely on its intrinsic nerve cells; but rather that the normal double tone control of the two systems can under altered circumstances be carried on with greater or less efficiency by one system only.

To recapitulate: rhythmic activity is an intrinsic property of involuntary muscle which becomes manifest when that muscle is in a condition of tone; this condition of tone is dependent upon both suitable chemical conditions and proper nervous control. The nervous control is normally dependent upon the integrity of two antagonistic systems of peripheral neurons but can also be maintained by one of these systems alone under certain conditions.

Bayliss and Starling seem to think that the combination of a preceding inhibition with a peristaltic contraction necessarily implies a true reflex action; it seems to me possible to give another explanation. The evidence shows that the inhibition is not due to any excitation of the inhibitory fibres in the splanchnics; but, as we know from many instances in the central nervous system, inhibition may occur in two ways, either by excitation of inhibitory nerves, or by inhibition of motor cells; also according to the whole of the evidence in this book the involuntary nervous system is built up on the same plan as the voluntary nervous system. Inhibition of motor cells in the former as well as excitation of motor cells is brought about by the action of connector nerves, as in the well-known instance of the reciprocal innervation of flexors and extensors either in the spinal animal or on stimulation of the pyramidal tracts through the cortex. So also in the case of the gut the same factors are present, motor nerve cells arranged serially in the gut wall and connector nerves—the vagus nerves—which by means of collaterals connect with these serially arranged motor nerve cells. If then the excitation of a connector nerve in the central nervous system can simultaneously excite one motor neuron and inhibit another, the excitation of a vagus nerve fibre in the gut may reasonably be able to excite one motor neuron in the gut and simultaneously inhibit another one.

Bayliss and Starling point out that stimulation of the vagus causes inhibition followed by increased movement, so that the

excitation of the vagus fibres does bring about both inhibitory and motor effects in the gut. It seems to me possible therefore to explain the myenteric reflex by the direct stimulation of the connector fibres of the vagus; but the connector neurons, of which these fibres are the axons, are situated in the medulla oblongata and are excited by sensory neurons in the central nervous system, so that in the isolated intestine they could not be excited by any local sensory neurons, if such existed. If then, as appears to be the case, stimulation of the connector fibres of the vagus is an important factor in this so-called reflex, such stimulation can only be brought about by the direct excitation of such fibres, due to the bolus or to the pinch, and not by any sensory neurons in the gut itself.

Taking all these facts into consideration it seems to me very advisable to suspend judgment upon the question whether or no a true reflex takes place in a special enteric nervous system, until the factors concerned have been much more carefully worked out than has been done at the present time.

CHAPTER IX

THE INNERVATION OF GLANDULAR STRUCTURES

ALL the nerves which cause secretion of duct-bearing glands belong to the involuntary system, and their motor neurons, like those to the involuntary muscles, all lie outside the central nervous system.

The duct-bearing glands may be divided into three sets according to their origin :—

1. Those derived from cells on the surface of the body, or epidermal glands, such as the sweat glands.

2. Those derived from cells in the surface of the gut, or endodermal glands, such as the pancreas, liver, etc.

3. Those derived from cells of the surface of the coelom, or mesodermal glands, such as the kidney.

It is generally stated that the epidermal glands are formed by invagination of the surface epithelium, so that one would naturally suppose that their innervation could not differ from that of the surrounding epithelial cells, which have not been invaginated. These latter are not known to have any connexion with efferent or motor nerve fibres but only with afferent or insensory fibres, and it is inconceivable that the mere act of invagination should alter the nerve supply. We should expect then *a priori* that such glands would be innervated from fibres belonging to the sensory rather than the motor part of the nervous system ; yet the evidence is very strong that, both in the case of the sweat glands and the prostate gland, secretion can be brought about by the stimulation of anterior and not posterior spinal roots. On the other hand it is possible that these cells, which are invaginated, are not the same as the surrounding cells, but were special glandular cells before invagination, which, though situated in the epiblast, were connected with the motor side of the nervous system, an innervation comparable to that of certain unstriped muscle cells which are also said to be derived from epiblast. In

both the cases cited the gland cells are very largely surrounded by unstriped muscle, so that, as already mentioned, the contraction of such muscle must squeeze out a secretion already formed. It is not however possible to explain all glandular secretion brought about by stimulation of a nerve as due to the squeezing action of contractile tissue.

The classical example of nervous action upon gland cells is the action of the chorda tympani on the secretory activity of the submaxillary gland. It has been shown conclusively that stimulation of this nerve, which is a branch of the facial nerve, causes a marked flow of saliva along Wharton's duct from the gland, and further that it consists of small medullated fibres which connect with cells of the submaxillary ganglion. This ganglion is situated close to the gland, and sends secretory fibres into the gland itself. In every respect the innervation is so similar to that of involuntary muscles, as to compel us to look upon these secretory nerve cells as belonging to the same system as the motor nerve cells of the involuntary system.

Further, the evidence seems to me conclusive that the fibres from these cells are true secretory nerves, for, apart from the actual flow of the secretion, marked histological differences occur in the gland cells according to whether they have been caused to secrete by nerve stimulation or are at rest. Also Barcroft has shown that active metabolism of the gland cells does take place on stimulation of the chorda tympani, for a largely increased amount of oxygen is taken in, in consequence of the nerve stimulation. Stimulation of the chorda causes also a large increase of the flow of blood through the gland, and it might possibly be argued that this increased flow causes the metabolism of the gland cells and not any direct action of secretory nerves. Barcroft and Müller have however shown that the injection of yohimbin will cause a tenfold increase in the blood-flow through the gland without any secretion of saliva, and that such increase does not cause any measurable change in the oxygen used by the gland. The gland after such treatment responds to stimulation of the chorda tympani with a good secretion of saliva accompanied by a sevenfold increase in the oxygen taken up. We must therefore include true secretory nerve cells and nerve fibres in the involuntary nervous system, and the chorda tympani and similar nerves must be classed with the other cerebro-spinal nerves as

containing the connector fibres connecting such cells with the central nervous system.

In addition to these secretory cells belonging to the bulbar outflow, the evidence points to the conclusion that a second outflow of secretory cells to the same glands has taken place along with the thoracic outflow. Stimulation of the cervical sympathetic nerve causes a distinct secretion of saliva, especially in the cat, and this secretion is accompanied by changes in the appearance of some of the gland cells indicative of activity. According to Barcroft and Piper adrenaline, when injected into the circulation, causes a flow of saliva, which is accompanied by a dilatation of the blood vessels of the gland and by a considerable increase in the metabolism of the gland as judged by the intake of oxygen. They argue that this increased metabolism cannot be accounted for by the stimulation of contractile tissues in the gland, for the amount of such tissue is too small to account for the extent of the metabolism. They therefore conclude that adrenaline produces a true secretion of the gland cells. Further ergotoxine, which paralyzes, as Dale has shown, all the motor activities of the sympathetic system, paralyzes also the secretory activity of that system, but not that due to stimulation of the chorda tympani; on the other hand atropine, which stops the flow of saliva obtained by stimulation of the chorda, does not affect the flow due to sympathetic stimulation unless the dose is very great.

This double supply of secretory nerve fibres has been shown for all the buccal secretory glands, parotid, submaxillary, sublingual, retro-lingual, also for such glands as the orbital and lacrymal; and in all cases the secretory nerves, which belong to the sympathetic system, arise from nerve cells in the superior cervical ganglion.

What is the meaning of this double innervation of these glands? I have already argued that we must, according to our present knowledge, accept a double innervation of involuntary muscle by motor and inhibitory fibres; it would seem then *a priori* natural that gland cells should possess a similar innervation. Heidenhain has argued that such is the case: the one set of fibres (sympathetic set) he called trophic and the other secretory, the trophic fibres being concerned with the formation of the secretory material in the gland and the others with the act

of secretion. The evidence at the present time is distinctly against this view, for both nerves cause apparently the same kind of metabolism in the gland cell, and both nerves can cause a secretion. If then we are bound to conclude that there is no real difference in the function of the two nerves, how can we explain the double innervation? The simplest explanation to my mind is that the nerves supply with secretory fibres glandular structures which are different morphologically, part being epidermal skin glands like the sweat glands and part being endodermal glands like the gastric and pancreatic glands. The former being supplied by sympathetic fibres would be affected by adrenaline and ergotoxine, while the latter would be supplied by connector nerves from the facial and glossopharyngeal nerves belonging to the bulbar group.

Langley states that, after long-continued stimulation of the chorda tympani, there are always gland cells to be found in the condition of rest upon microscopical investigation. This fact points to the conclusion that there are gland cells which are not innervated by the chorda tympani; the same reasoning applies also to the sympathetic. As yet no one has attempted to find out whether the gland cells affected either by adrenaline or stimulation of the sympathetic nerve are always the same and can be plotted out into definite groups. When we remember how definitely the Islets of Langerhans in the pancreas have been dissociated from the pancreatic cells themselves as the result of long-continued patient research, it is quite possible that similar research may succeed in differentiating between gland cells supplied by the chorda tympani and sympathetic nerves respectively. At present we do not know enough about the development of these glands or about their phylogenetic origin to be able definitely to say whether they belong to the endodermal or the epidermal group of glands or to both. It is possibly of significance that the two foremost gills in Ammocœtes, those belonging to the facial and glossopharyngeal segments, are markedly differentiated from the rest of the gills by the large amount of mucous glands in them, which have taken the place of the respiratory epithelium; indeed the gills of the foremost or facial respiratory segment have almost entirely lost all trace of respiratory epithelium and become converted into mucous glands.

The existence of secretory nerves for the gastric glands has been placed beyond question by the work of Pawlow. He

pointed out that the secretion of gastric juice which can be evoked by the presence or smell of food does not occur after section of the vagi nerves, and that stimulation of the peripheral end of the cut vagus nerve will cause a flow of gastric juice provided that too much anæsthetic has not been given. There is no evidence that the splanchnic nerves have any effect on the secretion of gastric juice.

The innervation of the pancreatic glands is not so clear as that of the gastric glands, because the stimulation of such a nerve as the vagus, which causes a flow of pancreatic juice, causes at the same time a secretion of gastric juice, and Bayliss and Starling have shown that the presence of the acid of the gastric juice in the duodenum causes an internal secretion from the cells of the duodenal mucous membrane of a substance, secretin, which on reaching the pancreatic gland produces a flow of pancreatic juice. For this reason it is not so certain that stimulation of the vagus nerve produces pancreatic secretion as the result of the excitation of nerve cells which send secretory fibres to the pancreas. Pawlow however has shown that, if the stomach be ligatured off and its contents made alkaline, stimulation of the vagus will still cause a secretion of pancreatic juice, which is very much less in extent than that seen when there is free access of gastric juice to the duodenal membrane. We must conclude that there are secretory nerves for the pancreas which arise from nerve cells connected with vagus connector nerve fibres. As to the splanchnic nerves, the evidence that they contain secretory fibres for the pancreas is still more doubtful.

I have already referred to the prostate gland in connexion with the muscular tissues surrounding it. According to Barrington there is some evidence that in the case of this gland as well as in that of Bartolini's and Cowper's glands, the same question of double innervation occurs, as has already been discussed at the anterior end of the body. He shows that the mucous secretion of Cowper's glands and of Bartolini's glands is controlled by the hypogastric nerves, the secretory nerve cells being situated peripherally and not in the inferior mesenteric ganglion, since the effect of stimulation of the hypogastric nerve is abolished by degenerative section of the inferior splanchnic nerves. He also finds that these glands are made to secrete by stimulation of the pelvic nerve, but to a much less extent than by stimulation of the

hypogastric. The secretion of the prostate is undoubtedly brought about mainly by secretory fibres in the hypogastric, which, when stimulated, cause a steady continuous secretion, very different from the transitory secretion caused by stimulation of the pelvic nerve. It may, however, be possible that the pelvic nerve also brings about a true secretion and not merely an emptying of the gland by muscular squeezing. These glands at the posterior end of the body may also therefore be derived from the two sources, epidermal and endodermal, and thus have a double secretory nerve supply.

So far we may, I think, draw these conclusions from our present knowledge: (1) the nerve cells which supply secretory nerve fibres to purely epidermal glands, e.g. the sweat glands, all belong to the sympathetic system and are connected with the central nervous system by the thoracico-lumbar outflow of connector nerves. (2) The nerve cells which supply secretory fibres to the purely endodermal glands, e.g. gastric and pancreatic, all belong to the enteral system and are connected with the central nervous system by the bulbar (vagus) outflow of connector nerves.

At the two extremities of the body, where the endoderm and ectoderm come together, the ectodermal and endodermal glands are mixed together and two sets of gland cells may become fused together to form one gland, with the result that that gland is supplied with secretory nerves both from the sympathetic and enteral nervous systems.

As the result of a consideration of the glandular structures we thus arrive at the same conception of an original double segmentation throughout the length of the animal, a somatic and a splanchnic, and we again see that the glands supplied with secretory fibres from the sympathetic system belong to the somatic and not to the splanchnic segmentation, while those wholly supplied by the enteral nervous system are entirely splanchnic. At the extremities of the body where the two systems meet, a fusing of the two types of glandular structure has taken place, which is indicated by a double innervation.

The third class of glands are those derived from the surface of the coelom and consist of the kidneys. There is at present no evidence that such gland cells are under the control of the nervous system at all. There is evidence that the supply of

blood to the kidneys is under the control of the nervous system, and the nerve fibres, which pass into the kidney, can be largely traced to the blood vessels. At present we have no conclusive evidence of nerve fibres to the kidney cells themselves. The kidney cells secrete substances brought to them by the blood, and the activity of these cells is determined by the chemical nature of these substances.

Again, however, we find in the nephric organ evidence of the double segmentation upon which I have laid so much stress. As I have pointed out, the segmental excretory organ of the annelids becomes a double set with the formation of appendages, as is seen in Peripatus, the somatic set remaining in the body, and the other appendicular set forming the coxal glands. These two sets of nephric organs represent respectively the two segmentations, somatic and appendicular, so characteristic of the higher invertebrates ; in the vertebrate the somatic nephric organs form the meso- and meta-nephros while the appendicular nephric organs form the pronephros.

The evidence of embryology shows that the first formed nephric organs belong to a few segments immediately succeeding the branchial segments, and form the pronephros with the segmental duct and possibly the most anterior of the mesonephric organs. Subsequently, with the development of the animal, more and more segments are formed always posterior to those first developed, constituting more mesonephric segments and finally the segments of the metanephros. The pronephros is confined to the earliest segments because they represent the appendage bearing segments of the invertebrate ancestor ; afterwards in the vertebrate stage, with the elongation of the animal, meso-somatic segments were formed but no new appendages. Consequently in these new segments we find the formation only of mesonephros and metanephros, no longer of pronephros.

CHAPTER X

THE CONNECTOR NEURONS OF THE INVOLUNTARY NERVOUS SYSTEM

I COME now to the consideration of the cells in the central nervous system which give origin to the various outflows of connector nerves—the thoracico-lumbar, the bulbo-sacral and the prosomatic.

In Chapter I, I discussed the position of the motor, connector, and sensory neurons in the voluntary nervous system, and pointed out that they must be considered in the light of a double segmentation, which I have called the somatic and splanchnic segmentations. In my book on the "Origin of Vertebrates" I have shown how this double segmentation follows naturally from the double segmentation so characteristic of the higher invertebrates, formed by the body segments on the one hand, and the appendages on the other. The muscles of the somatic segmentation of the invertebrate have formed the corresponding longitudinal and dorso-ventral groups of muscles of the vertebrate; and the muscles of the appendages have become the muscles of the splanchnic segmentation. The latter in the prosomatic region forms the muscles of mastication, which have been derived from the muscles of the masticatory appendages; and in the mesomatic region they form the muscles of respiration and the associated facial muscles which are supplied by the facial nerve, and also the deglutition and respiratory muscles supplied by the glosso-pharyngeal and vagus nerves. These mesosomatic appendages, which were originally free respiratory appendages, as in Limulus, became internally situated, as in the scorpion group, and formed the commencement of the new alimentary canal of the vertebrate, which is unique among alimentary canals in the marked segmentation of its anterior end. The branchial chamber, so formed was originally closer to the anal end of the body, as can be inferred from the appearances of such ancient forms as Bothriolepis,

Drepanaspis, etc., and opened into the anus by way of a posterior or cloacal chamber, formed in the same manner as the anterior or branchial chamber.

Such a conception implies that in the original vertebrate the wall of the alimentary canal was segmented along its whole length. The conversion of a crawling animal into a swimming animal necessitated a greater mobility obtained by elongation of the animal. This was brought about by an increase in the number of segments between the head end and the tail end; such segments belonged to the somatic segmentation only because, the animal being now a vertebrate, no new appendages of the invertebrate type could be formed, and consequently no new appendicular or splanchnic segments. Elongation of the gut must however take place with the elongation of the body and be supplied with muscles. Such muscles must arise from those of segments already existing, and consequently the splanchnic segmentation of the gut would still be confined to the original branchial and cloacal segments, its musculature being supplied by the bulbar and sacral nerves.

Now the evidence which I have given in previous chapters of this book shows that the involuntary muscular system (leaving out for the moment the vascular muscles) also falls into two distinct systems; the one—epidermal—is supplied by motor fibres from motor cells of the sympathetic system, and the other—endodermal—by motor fibres from motor cells of the bulbo-sacral or enteral system. All the muscles supplied by motor fibres from the sympathetic belong to the former group if, as I believe likely to be the case, the sphincter muscles of the gut turn out to be epidermal, and are differentiated by the action of adrenaline; all the muscles supplied by motor fibres from the enteral system belong to the endodermal group and are differentiated by the action of acetyl-choline. The unstriped muscles under the skin, which form the dermal group, must belong to the somatic segmentation, and the endodermal muscles to the splanchnic musculatures. There is therefore a strong suggestion of a morphological differentiation in the involuntary musculature of the same kind as that in the voluntary musculature; in other words, both striated and unstriated muscle existed in both the somatic and appendicular segments of the invertebrate, from which the vertebrate arose; and therefore the characteristics of the two

segmentations, somatic and splanchnic, apply to the unstriated as well as to the striated muscular groups. Just as the somatic segmentation is manifest throughout the length of the animal by the segmental arrangement of the striated longitudinal muscles of the trunk region, so also it is manifested in the same region by the segmentally innervated unstriped pilo-motor muscles. Since new appendicular segments were not formed after the vertebrate stage had been reached, not only the striated muscles of the gut receive their motor supply from the bulbo-sacral nerves, forming the enteral nervous system, but also the motor cells which send motor nerves to the corresponding unstriped endodermal muscles have travelled out from the bulbo-sacral regions of the cord.

So far as connexions to the peripheral motor neurons are concerned, the thoracico-lumbar outflow of connector nerves terminates around the motor cells of the vascular and dermal muscles, while the bulbo-sacral outflow terminates round the motor cells of the endodermal muscles. What evidence is there for the position of the cells in the central nervous system which respectively give origin to these connector fibres?

The Connector Neurons of the Thoracico-Lumbar Region.

It has long been known that the thoracic region of the cord is distinguished from the regions above and below by the presence of two distinct groups of nerve cells, of which the one forms a marked lateral horn, with small cells, and the other forms the cells of Clarke's column, with large cells. I pointed out in 1885 that the distribution of these two groups of nerve cells corresponded closely with the distribution of the connector fibres to the sympathetic nerve cells, and I suggested that the cells of the lateral horn gave rise to these connector fibres. The truth of this suggestion was confirmed by the experiments of Anderson, who cut the cervical sympathetic nerve in young kittens, and allowed the animals to grow up; he then found a marked difference in the number of the cells of the lateral horn column in the upper thoracic region on the two sides. The side on which the cervical sympathetic nerve had been cut showed many fewer cells than the intact side. Many observers since then have come

to the same conclusion, so that this column of cells is now universally considered to give origin to the connector fibres to the motor neurons of the vasodermal muscles forming the sympathetic system. To use the nomenclature given in Chapter I for the voluntary system, these cells, with their prolongations, are the primary connector neurons of that system (Fig. 2, *b*.). The cells of Clarke's column on the other hand clearly give origin to the fibres of the direct cerebellar tract, and are to be looked upon as directly concerned with sensory impulses between the periphery and the cerebellum. They with their prolongations belong to the cerebellar relay system of connector neurons, and have no direct connexion with any excitor neurons.

The Connector Neurons of the Sacral Outflow.

When we examine the structure of the spinal cord in the region of the second and third sacral nerves, we see again a distinct mass of nerve cells situated laterally on the edge of the grey matter ; these appear to bear the same relation to the connector fibres of the pelvic nerve as those in the lateral horn of the thoracic-lumbar region to the connector fibres of the sympathetic. As yet the experiment has not been made of cutting the pelvic nerve in very young animals and seeing what change occurs in the sacral region of the cord in consequence of such section.

It seemed to me possible that some of these cells might give origin to fibres, which travelling up the cord for a short distance came out with the lumbar splanchnics, and thus gave origin in the sacral region to certain of the connector fibres of the sympathetic system. Dr. Elliott made the experiment of cutting the cord in the region of the last lumbar or first sacral nerve, and allowed time for degeneration of the supposed fibres, but could find no sign of any degeneration in the lumbar splanchnics. Similarly, section of the cervical cord above the thoracic region gave no sign of any degeneration in the thoracic splanchnics.

Clearly then the cells, which give origin to the connector fibres of the thoracic-lumbar outflow, are strictly confined to the same portion of the spinal cord, and the corresponding cells in the sacral region give origin entirely to the connector fibres in the pelvic nerve.

The Connector Neurons of the Bulbar Outflow.

In the region of the medulla oblongata the nerves to be considered are the vagus, glossopharyngeal and facial.

The sensory neurons of the vagus and glossopharyngeal nerves send root fibres into the medulla oblongata, which terminate round cells of connector neurons, and as in the spinal cord, many of these root fibres travel some distance before they reach their connector cells; these latter fibres form a bundle known as the fasciculus solitarius or the descending root of the vagus and glossopharyngeal, the fibres of which connect with nerve cells along the whole of its course.

Certain of the sensory root fibres of the vagus and glossopharyngeal end in some of the cells in the large group on the floor of the fourth ventricle, known as the dorsal nucleus of the vagus. From cells of this nucleus fibres pass into the vagus nerve, which cause on stimulation contraction of the bronchial muscles, inhibition of the heart and other phenomena, characteristic of the stimulation of motor fibres belonging to the involuntary nervous system (Fig. 3, *c*.). For this reason Edinger divides this dorsal nucleus into a sensory and motor part; this means nothing more than that sensory root fibres connect with its cells, and some of those cells send into the vagus fibres which connect near the periphery with motor neurons of the involuntary nervous system; in other words, this mass of dorsally situated cells are the cells of connector neurons, some of which connect receptor neurons of the vagus group with the excitor neurons of the same group belonging to the involuntary nervous system. The axons of others of these connector neurons in all probability pass to the cells of the nucleus ambiguus, and so connect receptor neurons of the vagus group with excitor neurons of the same group belonging to the voluntary nervous system (Fig. 3, *b*.), they thus enable primary reflexes in the voluntary nervous system to take place in these segments. In this respect these cells in the dorsal nucleus of the vagus resemble the posterior horn cells in the spinal segments. Now the shifting which takes place, owing to the opening out of the central canal in the medullary region, brings the cells of the posterior horn, as far as the splanchnic segmentation is concerned, in among the cells of this dorsal nucleus, as Edinger has shown; while at the same time, the

posterior horn cells belonging to the somatic segmentation remain closely contiguous to the fibres of the ascending root of the trigeminal.

I have already in Chapter I sketched out the peculiarities of the segmentation in this region as far as the voluntary nervous system is concerned, and have come to the conclusion that the cells of the connector neurons belonging to the splanchnic segmentation are situated in the dorsal nucleus of the vagus, and are continued into the spinal cord as a column of cells accompanying the fasciculus solitarius, the fibres of which terminate in these cells (Fig. 1).

The cells in the dorsal nucleus of the vagus are not all of the same kind, they form two distinct groups, a large-celled and a small-celled group. The smaller cells were discovered by Staderini and form a group of cells extending over the whole of the dorsal nucleus, which have been called the nucleus intercalatus of Staderini. We should naturally suppose that the small-celled group gave origin to the small medullated fibres of the vagus nerve, which form the connector fibres to the motor cells of the involuntary muscles belonging to the vagus system. The evidence available appears to support this view. The literature on the subject is given by Kidd and Molhant; the experimental work consists mainly of degenerative sections of the vagus nerve or spinal branches of it and the observation of signs of chromatolysis in the bulbar cell groups belonging to the vagus nerve. All observers are agreed that cells in the dorsal nucleus of the vagus give origin to centrifugal fibres, which form connexions with the motor cells of the enteral system, and more recent work, as pointed out by Kidd, places these cells in that small-celled part of the dorsal nucleus known as the nucleus intercalatus of Staderini. This nucleus then consists of the connector cells of this region belonging to the involuntary nervous system. It might therefore be considered, as Kidd holds, to represent in the medulla the intermedio-lateral cell column so characteristic of the thoracico-lumbar region of the cord.

The arrangement for these direct or segmental reflexes in the involuntary nervous system of the medullary region are of the same kind as in the thoracic region of the cord. There is however this difference; in the medulla oblongata we are dealing exclusively with the enteral muscular system as far as

concerns the connexion of central nerve cells with peripheral motor cells; in the thoracic region we were considering not the enteral but the sympathetic muscular system as far as concerns the connexion of central nerve cells with peripheral motor cells. It does not therefore follow that the nucleus intercalatus of Staderini, which constitutes the connector neurons of the enteral nervous system in the medulla, is strictly a continuation of the intermedio-lateral cell column in the thoracic region, which forms the connector neurons belonging to the sympathetic nervous system. The former cell group would be more strictly comparable to the connector neurons in the sacral region, which give origin to the connector fibres forming the pelvic nerves. At present we have not sufficient experimental evidence to enable us to speak accurately of the position of these sacral connector neurons.

On the other hand, if we take into consideration not only the motor cells which send motor fibres to the endodermal muscles but also the cells which send inhibitory fibres to those muscles, these cells belong mainly to the sympathetic system and the cells of their connector neurons are presumably situated in the intermedio-lateral cell group. I am inclined on the whole to look upon the primary connector neurons of the involuntary nervous system as forming a cell column of the same nature as the cell column of the lateral horn, just as I look upon the corresponding connector neurons of the voluntary nervous system as all derived from the cells of the posterior horn.

The evidence points to the following conclusions:—

1. The cells on the floor of the fourth ventricle, known as the dorsal nucleus of the vagus, are all connector cells belonging to the splanchnic segmentation and include those belonging to the involuntary as well as the voluntary nervous system.

2. The small-celled part (the *nucleus intercalatus* of Staderini) gives origin to the connector nerves of the involuntary nervous system, and the large-celled part with its continuation into the spinal cord in connexion with the sensory fibres of the fasciculus solitarius gives origin to connector fibres of the voluntary nervous system.

3. I conclude that these two sets of connector neurons enable primary or segmental reflexes to be carried out both in the involuntary and voluntary splanchnic segments. At the same time,

as Edinger suggests, some of the cells may be concerned with the secondary or relay system of reflexes.

There is another group of peripheral excitor neurons which with their connector nerves belong to the mesosomatic group, namely, the secretory neurons which give origin to the secretory fibres of the parotid and submaxillary glands. According to Kohnstamm, the cells which give origin to these nerve fibres form two groups, the superior and inferior salivatory nuclei, situated just dorsal to the facial nucleus and the nucleus ambiguus respectively, and give the reflex path for direct simple salivary reflexes. Close to these cells are found others which are the end-nuclei of the sensory fibres of organs of taste, and are connector neurons belonging not to a direct but to a relay system.

The axons of the cells of the superior salivatory nucleus pass into the nervus intermedius, and pass by way of the chorda tympani to end in the cells of the submaxillary ganglia and the other salivary ganglia belonging to the chorda tympani group. The axons of the cells of the inferior salivatory nucleus pass into the glossopharyngeal nerve and thence into the nervus tympanicus to end in the cells of the otic ganglion, which supplies secretory fibres to the parotid gland (Fig. 6). Thus these cells with their axons form the connector neurons between the secretory neurons of the salivary glands and the appropriate sensory neurons of the trigeminal, chorda tympani and glossopharyngeal. They thus enable simple reflexes in the involuntary nervous system to take place in these segments.

Connector Neurons of the Prosomatic Region.

The nucleus of the oculomotor nerve is a large nucleus made up of a number of nuclei, each of which gives origin to one of the eye muscle nerves. All these nuclei are composed of large cells, and with their axons form the motor neurons of the voluntary muscles belonging to the somatic segmentation in this region (Fig. 6). Close against these cells but frontal to them and usually described as part of the oculomotor nucleus, a well-defined group of cells is seen, which are strikingly smaller than those in the rest of the nucleus; this small-celled group is believed to give origin to the small fibres in the oculomotor nerve, which terminate in the ciliary ganglion. Hensen and Volcker, in their original experiments, mapped out by stimulation the different component parts of the

oculomotor nucleus, and found that contraction of the sphincter muscle occurred upon stimulation of the most frontal part of the nucleus. The physiological evidence thus agrees with the histological, that the connector neurons of the involuntary nervous system in the prosomatic region are situated close against the motor neurons of the voluntary somatic muscles of the same region.

CHAPTER XI

THE PHYLOGENETIC ORIGIN OF THE SYMPATHETIC NERVOUS SYSTEM

In all the higher vertebrates we find three characteristic groups of motor nerve cells, which have travelled out from the central nervous system to form the vagus, sympathetic and pelvic groups; but in the lowest fishes, the Cyclostomata, the only one of these three groups which has been clearly recognized is that belonging to the vagus. Along the whole of the intestine of Ammocœtes the vagus nerve can be traced, and in connexion with its fibres nerve cells are found in the walls of the intestine itself, right up to the end of the intestine proper. The intestine is characterized by the presence of the so-called spiral valve, and terminates in a chamber, the hind gut or cloaca, into which the segmental duct from the pronephric organ opens on each side. Upon this cloaca Dohrn has seen scattered nerve cells lying close on its surface. These he calls sympathetic, but clearly he uses the term vaguely and not as it is used in physiological writings. Dohrn's cells correspond in position to the cells of the pelvic plexus in higher vertebrates, and in my opinion indicate that group, and not any of the sympathetic group of cells. In the Ammocœtes then the cloacal and intestinal cell groups are both present in the same positions as in the higher vertebrates, and therefore in all probability the sympathetic system of cells must be present also in this animal.

It is impossible to consider the origin of the sympathetic nervous system in vertebrates, without taking into account the distribution of the chromaffine system of cells; for the two systems are closely bound up together. My son, J. F. Gaskell, has been investigating this relationship both in vertebrates and invertebrates. In the adult mammal the chromaffine system is confined to the medulla of the suprarenals, but in the embryo chromaffine cells are found in close connexion with

sympathetic cells ; a specially large mass known as Zuckerkandl's body, which is found at the bifurcation of the abdominal aorta, lasts till birth, closely connected with the inferior mesenteric ganglia. As we pass downwards in the animal kingdom, we find the chromaffine cells and the sympathetic cells in close contact, even in the adult condition. In the Amphibia, where the sympathetic ganglia are arranged much in the same way as in the Mammalia, the chromaffine cells and the sympathetic cells are mixed close together in every ganglion. So also in the Elasmobranchs, the intimate juxtaposition of the chromaffine cell masses and the sympathetic ganglia has been long known, and the origin of both from a common mass of cells was first described by Balfour.

In the Dipnoi, Teleostei, Ganoidei and Cyclostomata, Giacomini has shown that both systems lie in intimate connexion with the cardinal and segmental veins, also that the relationship between individual cells of the two systems is often extremely close, a ganglion cell lying in close contact with a group of chromaffine cells.

The more primitive the animal the less conspicuous becomes the sympathetic system. It is, according to Giacomini, present in the Dipnoi, mainly in the form of two very fine lateral chains ; but in the Teleostei, Ganoidei and Cyclostomata, it is not yet aggregated into definite regular chains, but its cells are scattered in irregular groups about the veins in company with the chromaffine cells, the component cells being still fairly numerous in the Teleostei, less numerous in the Ganoidei, and extremely few in the Cyclostomata.

In the lowest group of vertebrates then the sympathetic cells are so few that they cannot be described as forming a system ; their place is taken by the masses of chromaffine cells, which form a scattered but segmentally arranged system in the very position occupied in the higher animals by the sympathetic system.

In Petromyzon, groups of chromaffine cells are found in every segment in exceedingly close contact with the cells of the posterior root ganglion, where the segmental vein comes close against that ganglion ; scattered groups of cells are found along the walls of the segmental vein to its junction with the cardinal vein and along the cardinal vein itself ; also a few are found along the peripheral branches of the segmental vein. My son finds these

cells in all cases in close relationship with the segmental nerves from the posterior root ganglia. Where the cardinal veins fuse together to form the sinus of the heart, the chromaffine cells form a mass on the dorsal wall of the sinus, and extend over the walls of the cœliac artery, which passes through the sinus obliquely. In the branchial region the chromaffine cells are found along the segmental veins up to the second branchial segment, but much more sparsely than in the segments posterior to the heart. Headwards of this limit no chromaffine cells have been found in connexion with any segment.

Comparative anatomy thus shows most clearly the close relationship between the chromaffine and sympathetic systems, and the remarkable increase in the latter system, apparently at the expense of the former, which has taken place, commencing in the lowermost groups of vertebrates.

Embryology emphasizes in the most positive manner the close relationship between the two systems. Kohn has shown that the sympathetic ganglia and the chromaffine cells arise in the embryo from a common mass of cells, part of which gives rise to the sympathetic ganglia and the rest form chromaffine cells; so intimate is the relationship according to his researches that he has given the name of paraganglia to the various groups of chromaffine cells.

Combining then the evidence of Kohn with that of Onodi it follows that the cells which gave origin to both the sympathetic and chromaffine systems of cells were originally in close contact with the posterior root ganglia, and have travelled out from that position. The truth of the Law of Recapitulation is shown yet again by the relationships found in the lowest vertebrates—the Cyclostomata—where masses of chromaffine cells still retain that position even in the adult animal.

The physiological evidence points in the same direction as the embryological, for the work of Elliott and others has shown that a discharge of adrenaline with a consequent rise of blood pressure takes place through the action of the splanchnic nerves; therefore the activity of these cells in the medulla of the suprarenal glands can be brought about by excitation of the fibres of the splanchnic nerves, which go to the suprarenals. Further he has shown that the fibres which pass into the suprarenals from the splanchnics are all medullated fibres, and are therefore

according to my nomenclature, either connector or sensory fibres. It is, however, very difficult to find any true nerve cells among the mass of chromaffine cells which constitute the medullary portion of the suprarenal; certainly the number present is quite insufficient to account for the number of splanchnic medullated fibres which pass in. If we accept the embryological evidence that these chromaffine cells are modified sympathetic nerve cells, then the medullated fibres of the splanchnic are naturally the connector fibres to these modified sympathetic nerve cells, and the absence of a sufficient number of true ganglion cells is accounted for.

Smirnow in 1890 investigated the structure of the nerve cells in the sympathetic of Amphibians, and found that, in addition to true nerve cells, nests of peculiar cells were always present in the sympathetic ganglia. He also found that the nerve fibres going to and from these cell nests resemble in their arrangement those going to and from the neighbouring nerve cells so closely as to cause him to assert that these structures are nests of sympathetic nerve cells, and he suggests that their peculiarities may be accounted for on the supposition that they are sympathetic cells in a young stage. He did not know of the chromaffine cells at that time. Clearly these cell nests are the chromaffine cells so universally found in the sympathetic ganglia of Amphibians, and Smirnow's observations show that these cells behave like sympathetic nerve cells in the arrangement of their nerve fibres.

Further there is some histological evidence which points in the same direction. Macallum, at the meeting of the British Association in Birmingham, showed that in sections of perfectly fresh material, cut frozen and put into a solution of nitrate of silver, all nerve cells took on a black staining, the most intensive colour being in the cells of the sympathetic system. No other tissues in the body were blackened except the medullary cells of the suprarenal, which were stained as deeply as the cells of the sympathetic ganglia.

Again there is evidence that the action of sympathetic nerves to the vascular musculature is dependent on a supply of adrenaline. Elliott found that excision of the suprarenal glands brought about the death of the animal in a short time owing to the great fall of blood pressure and marked weakness of the

heart's action thereby induced. This is exactly what is seen also in Addison's disease, where with the progress of the disease of the suprarenals a progressive fall of blood pressure and weakness of the heart are invariable symptoms. This evidence shows that the sympathetic nerves alone, although connected with the central nervous system and not interfered with, are unable to keep up the tone of the vascular system in the absence of adrenaline. Indeed Elliott found that in animals, moribund in consequence of removal of the suprarenals, the tissues supplied by sympathetic nerves may even fail to respond to electrical stimulation of such nerves, although the nerves of external sensation and those controlling the skeletal muscles are perfectly efficient.

In the case of the lowest vertebrate, Petromyzon, the segmental anterior nerves run separately from and alternate with the segmental posterior nerves, and supply only the segmental somatic muscles. On the other hand segmental posterior nerves accompany the blood vessels and are apparently distributed with the various vascular branches throughout the body. Again a marked acceleration of the heart in the lamprey takes place upon the administration of adrenaline, and also, as my son has found upon exposure of the spinal cord at the end of the branchial region ; the cord having first been isolated, but left in nervous connexion with the heart. Considering the very small number of sympathetic cells found in the lamprey and the great mass of chromaffine cells, especially on the sinus of the heart, we can only conclude that the motor regulation of the vascular system of this animal is carried out by the chromaffine system more than by the sympathetic system.

The whole evidence points strongly to the conclusion that the three systems, vascular muscular system, chromaffine system, and sympathetic system, are very closely interdependent. Striking evidence of this is afforded by Amphioxus, where there is no evidence of any vascular muscular system, and at the same time no sign of either sympathetic nerve cells or of any chromaffine tissue.

The evidence of the lowest vertebrate thus points to the origin of the sympathetic nervous system from nerve cells in the central nervous system of some invertebrate, which are motor to the vascular system and contain adrenaline in their substance. In my book on the " Origin of Vertebrates," I have given my reasons

for the belief that the vertebrates arose without reversal of surfaces from the Palæostraca—forms which were neither Crustaceans nor Arachnids, but gave origin to both ; forms which were much more nearly allied to the worms than are the crayfish and spiders of the present day ; and the resemblances which I have put forward are based partly on the anatomy of such animals as king crabs and sea scorpions, partly on the structure of worms.

It is therefore a striking fact that Poll and Sommer found certain chromaffine nerve cells, probably therefore containing adrenaline, in the central nervous system of worms. Further investigation on this matter has been carried out by my son. He searched in a large number of Annelids and Crustaceans for signs of chromaffine tissue in some organ or other, and arrived at the conclusion, that the adrenaline is confined to certain nerve cells in the central nervous system of certain Annelids. In the Crustaceans examined by him he found no sign of chrome staining in any cells of the central nervous system. He did not however carry the investigation to tissues outside the central nervous system, therefore the presence of chromaffine cells outside the central nervous system in invertebrates has not been excluded. These cells give a most marked reaction, and in all Annelids investigated by him, in which they occur, are invariably three in number on each side of a ganglion and constant in position. He has found them in the Hirudineæ, Lumbricus Herculeus, Aphrodite Aculeata and Eunice Gigantia. In all cases, where he has found them, it is striking to see how well developed are the muscles of the vascular system ; where the reaction is not to be seen, as in most of the sea-living Polychætes, true vascular muscles do not appear to exist. These observations point strongly to the conclusion that these three cells on each side in each ganglion have to do with the innervation of vascular muscles.

In Hirudo and Aulostoma the most ventrally situated of these three cells on each side of any ganglion of the ventral chain is a colossal cell, so that there are in each ganglion two of these colossal cells, which are so much bigger than any other cells in the ganglion that they cannot be mistaken however they are stained. In all cases, where these colossal cells occur, they stain with chrome salts and probably contain adrenaline. It might be objected that enormous cells like these cannot send motor fibres

to such small muscle fibres as those in the blood vessels ; but as already mentioned, in the invertebrate central nervous system, one large nerve cell supplies with motor nerves a great quantity of muscles by means of continual division of its motor fibre before it reaches the muscles, so that a large nerve cell may indicate the innervation by it of a large number of muscles even though they are small in size.

Another striking peculiarity of the cells in the ganglia of the leech has been observed. Retzius has examined the cells in the ganglion of the leech by the methylene blue method, and given illustrations of the course of the axons of the cells in the ganglion. Each ganglion gives origin on each side to two nerves, an anterior and a posterior nerve, and the nerve fibres from many of the cells can be traced into one or other of these two nerves. In the group of the leeches, Retzius finds that there are nerve cells on each side, whose axis cylinder process divides into two in the ganglion itself, and of the two fibres so formed, the one passes into the anterior nerve and the other into the posterior nerve. One of such cells is the colossal cell. One then of these cells with splitting processes is certainly the same as a cell containing adrenaline.

The contractile vessels of the leech beat with great regularity ; and my son has been unable to find any ganglion cells in their walls, though he has traced nerve fibres to them from both the anterior and posterior nerves. By the use of curare, which paralyzes both the longitudinal and circular muscles of the leech, he has been able to see the effect upon the rhythm of the longitudinal vessel of stimulation of the anterior nerve and posterior nerve respectively, and has found undoubted acceleration upon stimulation of the anterior nerve but never on stimulation of the posterior nerve. The effect in the latter case was irregular and generally doubtful in curarized leeches, but in non-curarized leeches slowing was always obtained; the slowing was in some cases very well marked, but never reached to absolute stoppage of the beats. Curare therefore affects the inhibitory mechanism, just as it does in the vertebrate heart, masking its effect. Certainly the heart of the leech is affected by muscarine and atropine in the same way as in the vertebrate : muscarine will cause absolute stoppage which can be recovered from by a subsequent dose of atropine. Finally adrenaline in a neutral solution (adrenaline

borate) causes well-marked acceleration when applied to the longitudinal blood vessel.

He has also discovered another remarkable characteristic in connexion with the adrenaline in these cells; if the living ganglion is stained with methylene blue, the ganglion cells and their processes take on a blue coloration, the number and position of the cells thus coloured varying in different experiments; this coloration is not permanent but soon begins to fade. If however a solution of a chrome salt be inserted under the cover slip when the blue coloration is most distinct, then all the cells and nerve fibres decolorize almost immediately with the exception of the three cells containing adrenaline, which remain blue and are still blue even on the next day. Ultimately they too lose their colour. This more permanent blue coloration is not confined to the nerve cell but extends some distance along the axon of the cell. The reaction is evidently dependent on the presence of adrenaline, and it shows therefore that the adrenaline is not confined to the body of the cell, but extends into the axon as well.

In the case of the medullary cells of the suprarenal gland, the adrenaline is discharged from the cell into the surrounding fluid by the action of fibres of the splanchnic nerve; it is just possible that in the case of the leech the adrenaline passes from the cell to the periphery by way of the motor nerve itself. If such a suggestion prove to be true it opens out a new and most important chapter in our conceptions of the nature of nervous action.

Of equal or even greater importance for neurology is the discovery that one nerve cell sends a nerve fibre into each of two separate outgoing nerves by means of a splitting of its axon within the central nervous system. A similar supply of two nerve fibres from a single cell to separate nerves is indicated also in the Crustacean central nervous system, so that such an innervation appears not to be uncommon among invertebrates. In the same invertebrates the motor nerves to muscles of one function seem to run in a separate nerve from those to the antagonistic muscles; thus Hardy's work showed that in the Crustacean the motor nerves to the flexors were grouped in one nerve and those to the extensors in another; and my son finds that stimulation of the anterior nerve in the leech causes contraction of the

circular and dorso-ventral muscles, while that of the posterior nerve causes the antagonistic muscles, the longitudinal muscles, to contract.

Muscles and their antagonists are then very apt to receive their motor supply from the central nervous system by way of nerves which run separately ; but a muscle and its antagonist are necessarily bound closely together in their innervation, which is of a reciprocal character, so that the contraction of the one muscle is accompanied by the inhibition of the other. If then it is found that the axon of a nerve cell in the central nervous system splits to form two nerve fibres, one of which passes out into one nerve and the other into a quite separate nerve, it seems impossible that both those fibres should be motor to muscles of the same group, and much more probable that they supply antagonistic muscles with efferent nerve fibres of opposite character.

The origin of reciprocal innervation is on this scheme to be found in a single excitor neuron, which innervates a muscle and its antagonist in opposite directions by means of the splitting of its axon. Such cells may well reciprocally innervate such muscles as the voluntary circular and longitudinal muscles of the leech, the motor fibres of which run respectively in the anterior and posterior nerves.

My son has also observed the cells with splitting processes, which Retzius described, and finds that the smaller lateral cells with such processes do not coincide with the lateral adrenaline cells. Preparations clearly demonstrating these splitting fibres are only occasionally obtained, and the number of such cells is therefore difficult to determine. Retzius only described two, situated laterally ; and undoubtedly two cells, staining exceptionally easily, whose axons split in the ganglion, can sometimes be seen in a single preparation. There are however indications that other cells also have fibres which split in the same manner, whose identification is much more difficult, as the staining of more and more cells renders the picture more confused. The lateral adrenaline cells stain badly and very late, so that identification of any splitting of their axons in the ganglion is a matter of extreme difficulty. The chief fact that emerges is that two or more cells exist, which do not contain adrenaline but supply both anterior and posterior nerves with efferent fibres.

A similar reciprocal innervation for the musculature of the

vascular system is suggested by the behaviour of the colossal adrenaline cell, which also sends efferent fibres into the anterior and posterior nerves, but the relationship between the three adrenaline containing cells is not yet known, nor indeed is it quite certain that the axons of the other two cells behave in the same way as that of the colossal cell. One striking fact is common to the axons of cells which split in the ganglion to form two fibres: after splitting one fibre is invariably bigger than the other. This fact is very suggestive when considered in conjunction with Biedermann's statement that the nerves to the antagonistic muscles of the cray-fish claw show, near their termination in the muscle, the existence of two nerve fibres in the same sheath, which always branch simultaneously in their path to the muscle: the one fibre is invariably larger than the other. The larger of these two fibres is usually held to be the motor fibre and the smaller the inhibitory fibre to the muscle.

If such an excitor neuron has travelled out of the central nervous system towards the periphery in one of the outflows of the involuntary nervous system, it would by itself effect the reciprocal innervation of antagonistic muscles in that system, and give an efficient explanation of the numerous instances, already given, of the presence in the same ganglion of neurons motor to one group of muscles and inhibitory to the other.

Considerable difficulties beset the view, that a single nerve cell supplies a motor nerve fibre to one muscle, and an inhibitory nerve fibre to the opposing muscle, in those cases where there are only two outgoing nerves, into which these fibres respectively pass. It would follow that the one nerve would contain both the motor and inhibitory fibres to the one muscle and the other nerve both the motor and inhibitory fibres to the opposing muscle, but Celesia's evidence in the cray-fish makes us believe that stimulation of the one nerve excites the one muscle and simultaneously inhibits the opposing muscle, so that the inhibitory nerves of the one muscle leave the central nervous system with the motor nerves of the opposing muscle. My son has seen indications of the same phenomenon in the case of the longitudinal and circular muscles of the leech. At present we have not sufficient evidence to enable us to explain the meaning of this striking phenomenon of the invertebrate central nervous system, viz.: the origin from one nerve cell of two nerve

fibres which pass out from the central nervous system into two separate nerves respectively innervating with motor fibres antagonistic muscles.

The muscular system, whose motor fibres arise from cells of the sympathetic system, and which I have called shortly the sympathetic musculature, appears in the first instance, judging from the evidence of the annelids, to have been confined to the vascular musculature; whether it has spread from there to form a sheet of muscle underlying the epidermis or whether the dermal musculature has nothing to do with that of the blood vessels is a question of great interest which must be left for future research.

I would further venture to suggest that the same kind of nerve cell may be the essential factor in the reciprocal innervation of muscle belonging to the voluntary system of the vertebrate, with the difference that it is not situated in the excitor neurons of that system. There is no evidence at present that inhibitory nerve cells and fibres exist in the voluntary nervous system; reciprocal innervation of antagonistic muscles is due to the excitation and inhibition of the motor neurons themselves, and not to direct action on the muscles.

Sherrington's work has shown clearly how this reciprocal innervation can be maintained by the spinal cord alone, and he has established the laws of this reflex action. It can be carried out by the direct reflexes in the spinal cord involving the simple reflex arc of receptor, connector and excitor neurons. As the excitor neurons send only motor fibres to the muscles, we must look for the mechanism of the reciprocal innervation in the connector neurons, and search for evidence that they are connected with motor neurons by two sets of fibres, of which the one excites and the other inhibits the activity of the appropriate motor neurons.

CHAPTER XII

SUMMARY

In the previous chapters I have taken separately and examined in detail the various systems of involuntary muscles, which occur in vertebrates, and also the various nervous groups or systems which are connected with them. In this final chapter I will attempt to shortly put together all these systems and give my present views on their inter-relationships and possible evolution.

The unstriped muscles of vertebrate animals belong to certain definite groups characterized by their innervation and by response to certain substances formed naturally in the body. I recognize the following groups of muscles :—

1. A vascular group.

2. A group of muscles underlying the skin or epidermis, which I have called the dermal or ectodermal musculature.

3. A group of muscles underlying the surface of the gut or endoderm, which I have called the endodermal musculature.

4. A group of muscles around the segmental duct.

5. A group of muscles forming part of the gut walls which especially constitute the system of sphincter muscles.

6. A group of muscles connected with the adjustment of vision.

The motor nerves of all these muscles arise from nerve cells which are situated, not in the central nervous system, as in the case of all striated muscles, but in the periphery. Further taking the first five groups these can be arranged definitely into two groups: 1, those which contract in the presence of a very minute amount of adrenaline, and 2, those which contract in the presence of a still smaller amount of acetyl-choline. The groups 1, 2, 4, 5, are all united into one group, which may be called the adrenaline group, while 3, the endodermal musculature, forms alone the acetyl-choline group. The striking action of these two substances, adrenaline and acetyl-choline, is correlated with the

differences in the innervation of these two groups of muscles. For if we make use of the term nervous system to designate these peripheral nerve cells and their nerve fibres, we see that these two groups of muscles are supplied by motor fibres from two distinct nervous systems. The first I designate the "sympathetic nervous system" retaining the old name and the other the "enteral nervous system." The adrenaline group of muscles is supplied by motor fibres exclusively from the nerve cells of the sympathetic nervous system, and the endodermal group of muscles from those of the enteral nervous system. The nerve cells of these two systems cannot all be considered to be motor, for in the involuntary nervous system I accept the existence of inhibitory nerve cells and nerve fibres as well as motor nerve cells and fibres; the nerve cells therefore of both the sympathetic and enteral nervous systems include inhibitory and motor nerve cells, which supply respectively inhibitory and motor nerve fibres to unstriped muscle.

Further the motor nerve cells of these two nervous systems are connected with the central nervous system, and their connector nerves are confined to certain regions of the spinal cord forming three marked outflows, which I have called the bulbar, thoracico-lumbar and sacral outflows. The distinctiveness of the sympathetic and enteral systems is again made manifest, for the connector fibres to the nerve cells of the sympathetic system are confined to the thoracico-lumbar outflow, and those to the nerve cells of the enteral system to the bulbo-sacral outflow.

Embryological investigations show that the nerve cells of both these systems were originally in the central nervous system and have travelled out from it. In that travelling out the sympathetic cells have been accompanied by cells containing adrenaline. These latter form the chromaffine system of cells, and the close relationship found always to exist between chromaffine cells and sympathetic cells, both from an anatomical as well as from a physiological standpoint, strongly suggests their common origin from a definite group of adrenaline containing nerve cells in the central nervous system of the ancestor of the vertebrate. Such nerve cells exist in the central nervous system of those segmented annelids which possess a muscular vascular system. They are well seen in the leeches and represent in my opinion the origin of both the sympathetic and chromaffine cells of the vertebrate.

In the lowest vertebrate (Ammocœtes) they have left the central nervous system mainly as chromaffine cells, and masses of them are still found close against the cells of the posterior root ganglia, with which the embryology of the higher vertebrates shows that the sympathetic nerve cells leave the central nervous system. As we pass from the lowest to the highest vertebrates the sympathetic cells become more numerous and the chromaffine cells diminish in number, until at last in the mammalia the sympathetic system is fully developed and the chromaffine system reduced to the cells found in the medulla of the suprarenal capsules.

The evidence of embryology and comparative anatomy thus points strongly to the conclusion that the sympathetic nervous system arose from nerve cells containing adrenaline, such as are found in the central nervous system of all segmented annelids which possess vascular muscles, and that, when these cells left the central nervous system to become peripheral, they left not as single cells but as two separate cells one of which contained all the adrenaline and formed the chromaffine system, and the other the nerve cells of the sympathetic system of the vertebrate.

These nerve cells, which have travelled out from the central nervous system, include inhibitory as well as motor cells in both the sympathetic and enteral nervous systems : the usual rule appears to be that the inhibitory cells of the one system have travelled out with the motor cells of the other system and vice versa. The most perfect illustration of this is found, when the muscles of the two systems have become antagonistic in function, as in the case of the sphincter musculature and the endodermal musculature. The motor nerves of the sphincter group of muscles belong to the sympathetic nervous system, and their motor nerve cells have travelled out as far as the inferior mesenteric ganglia in the case of the sphincter system of the coprodœum and urodœum, and as far as the superior mesenteric ganglia in the case of the ileo-colic sphincter : the inhibitory nerves to the corresponding antagonistic muscles arise, in the case of the endodermal muscles of the bladder and large intestine, from nerve cells in the inferior mesenteric ganglia, and in the case of the small intestine from those in the superior mesenteric ganglia. The motor cells of the sphincter muscles and the inhibitory cells of the neighbouring endodermal muscles have therefore reached

the same peripheral ganglia: this fact suggests that they may have a close relation to each other, that they started as a single cell in the central nervous system, and that the axis cylinder split to form two nerves, one of which was motor to the one muscle, and the other inhibitory to the antagonistic muscle. It is a striking characteristic of the cells of the central nervous system of the leech that in some of them the axis cylinder does split into two fibres, which pass out of the central nervous system in separate nerves supplying different groups of muscles. One of the nerve cells which is known to possess this peculiarity is one of the adrenaline containing cells, which I have suggested gave origin to the sympathetic nervous system. Further research is badly needed on the meaning of this peculiarity, which is such a marked feature in the central nervous system of the segmented annelid group.

With respect to the dermal system of muscles the motor cells all belong to the sympathetic system and are situated in the lateral chain of ganglia; the inhibitory nerve cells of these muscles are known in the case of the retractor penis muscles and of the muscles round the anus, and all belong to the enteral system; at present, however, we know nothing of any inhibitory nerves to the main mass of dermal muscles, which form the pilo-motor group.

The segmental duct system of musculature shows no sign of such reciprocal innervation; both motor and inhibitory nerve cells have travelled out as far as the musculature itself, and both belong entirely to the sympathetic system and are not connected in any way with the enteral system.

The vascular group of muscles, which is supplied with motor fibres from the sympathetic system alone, shows many signs of possessing a reciprocal innervation of the same character as in other cases; thus the dilatation of blood vessels, which causes erection, is brought about by the nervus erigens or pelvic nerve, a connector nerve belonging to the sacral outflow and therefore to the enteral system. In many other cases, where dilatation of vessels is brought about by stimulation of connector nerves of the bulbar outflow, it is always doubtful whether we are dealing with the inhibitory nerves to the muscles of the blood vessel, or whether the dilatation of the vessel may not be due to the influence of chemical substances formed by the activity of the organs con-

cerned, and not to any action of the nerve on the vascular muscle itself. In the case of the heart, where the vascular muscle is the organ itself, we see clear proof of the reciprocal innervation by the two systems, for the motor cells belong to the sympathetic system, and are situated in the lateral chain of ganglia, while the inhibitory cells are situated in the heart itself and belong to the vagus nerve and therefore to the enteral system.

I pass now to the musculature of the enteral system—the endodermal muscles. Their motor cells have travelled out as far as the muscles themselves, and in the case of the large intestine have been accompanied by the inhibitory cells of the sympathetic musculature, the pelvic plexus contains both the motor cells to the endodermal muscle of the large intestine and bladder as well as the inhibitory cells to the sphincter musculature of the same organs. Here again we see the same suggestion of the travelling out of a single nerve cell which gives origin to motor nerves to endodermal musculature and inhibitory nerves to opposing musculature. At present we cannot speak of the inhibitory nerve cells of the ileo-colic sphincter, for they have not yet been traced.

In other cases of endodermal musculature we find indications of reciprocal innervation between the enteral and sympathetic systems; thus the motor cells of the endodermal musculature, whether in the lungs (bronchial muscles) or in the liver (muscles of the gall bladder and duct), have travelled out right into the muscles themselves and their inhibitory nerves come from the nerve cells of the sympathetic system. The exception to the rule is found in the behaviour of the endodermal musculature of that portion of the alimentary canal which is anterior to the stomach. Here apparently both inhibitory and motor fibres belong to the enteral system, and the sympathetic does not send any fibres to it.

The fact that certain nerve cells in the central nervous system of segmented annelids contain adrenaline, and that the presence of such nerve cells is correlated with the presence of muscular tissue in the vascular systems, points most strongly to the conclusion that here in the annelid group we are watching the genesis of the sympathetic nervous system. My whole theory of the origin of vertebrates is based on an ancestor, which itself had arisen from the segmented annelid group, and on this

hypothesis the muscular groups of the vertebrate must have arisen from corresponding groups in the annelid ancestor. It is worth while here in this final chapter to give my views on the possible ways in which such conversion took place.

The fundamental hypothesis is that the central nervous system of the invertebrates has formed the central nervous system of the vertebrate by growing round and enclosing the alimentary canal of the former, so that the alimentary canal of the vertebrate is a new formation derived from structures already existing in the invertebrate ancestor. The most important fixed structure common to both the invertebrate and the vertebrate is the central nervous system with the nerves arising from it; those nerves are arranged in the same manner in the two groups of animals. First the supra-infundibular nerves, the optic and olfactory, correspond to the supra-œsophageal nerves, then the infra-infundibular nerves correspond to infra-œsophageal and give origin to the nerves of mastication and respiration, and finally the spinal nerves correspond to the nerves from the ventral chain of ganglia in the invertebrates. Further, the infra-infundibular nerves, which like the infra-œsophageal may be divided into a prosomatic and mesosomatic group (using the terms employed to characterize the foremost divisions of such animals as Limulus or the scorpion), are not built up of two roots as in the case of the spinal segmental nerves, one ventral and motor and one dorsal and sensory, but of three roots, one ventral and motor, one lateral, and one dorsal and sensory, the lateral root being both motor and sensory. Now the cranial region is older than the spinal region, so that this three-root system must be looked upon as the more primitive system, and indeed the two-root system can be derived from it by leaving out the lateral root. The lateral root nerves form a definite group of prosomatic and mesosomatic nerves, and supply with motor fibres the striated muscles of mastication (fifth nerve), respiration, deglutition and facial expression. This group of muscles is differentiated from other striated muscles in their origin, since they are all formed from muscles surrounding branchial and visceral arches, and represent the muscles of a distinct segmentation due to the branchial segmentation in the mesosomatic region, and a similar but non-branchial segmentation in the prosomatic region.

There is thus a double segmentation in the cranial region

which has been called branchiomeric and mesomeric, and by me splanchnic and somatic, so as to include the musculature of the non-branchial arches as well as the branchial.

A three-root system is found in the segmental nerves of Limulus and the scorpion, and one of the roots contains conspicuously both sensory and motor fibres and supplies entirely the appendage of each segment. Here also a double segmentation is recognized, due to body segments and appendage segments; the body segments form a somatic segmentation corresponding to that of the vertebrate, and the appendage segments would correspond to the splanchnic segmentation of the vertebrate if the masticatory and branchial muscles were derived from the muscles of the masticatory and branchial appendage of the invertebrate. The study of the lowest vertebrate, Ammocœtes, shows how natural it is to look upon the branchial unit as a buried branchial appendage, and leads to the conclusion that the branchial region of the new-formed alimentary canal was formed as a branchial chamber by a number of fused branchial appendages, the muscles of which have thus become the striated muscles supplied by the facial, vagus and glossopharyngeal nerves. At first the respiratory chamber so formed extended close up to a similar chamber, formed possibly by appendages, at the anal end of the body, and opened into that chamber; so that originally, as in the arthropods, the double segmentation due to appendages and body segments existed throughout the whole length of the animal. When the animal became a vertebrate with a smooth body surface and changed its locomotion from that of a crawling animal to that of a swimming animal, new segments were formed, by which greater mobility was gained; in these new-formed segments the appendicular segmentation would not be represented, and the new-formed gut would simply lengthen and its muscles would be supplied from those already formed.

At the time when the vertebrate first appeared, neither arthropods nor arachnids like those of the present day had been evolved. We must therefore regard the ancestor of the vertebrate as being much nearer the annelid stage, and can presume that his muscles were not all striated as in present-day arthropods, but some only had reached this stage, while others were unstriped. A living example of a very primitive arthropod is Peripatus, and here, as pointed out by Balfour, the muscles of

the foremost appendages only are striated, those of the rest of the appendages being unstriped; it is therefore reasonable to include unstriated muscle in the muscles of this appendicular segmentation and also in the splanchnic segmentation of vertebrates. Moreover in the vertebrate the motor nerve cells of all unstriped muscle have travelled out from the central nervous system to the periphery, so that the motor nerves of such unstriped muscle no longer form part of ventral or lateral roots; their original segmental position is nevertheless indicated by the outflows of connector fibres which connect these peripheral cells with cells in the central nervous system. Therefore, just as the ventral and lateral roots indicate the somatic and splanchnic segmentation of the voluntary muscular system, so also the same roots will indicate by means of the connector nerves the somatic and splanchnic segmentation of the involuntary nervous system. The thoracico-lumbar outflow of connector fibres is found in all the anterior roots of that region, showing that the dermal musculature belongs to the same somatic segmentation as the longitudinal striated muscles of the body. The bulbar outflow of connector fibres on the other hand is found in the lateral roots of the bulbar region, showing that the endodermal musculature belongs to the same splanchnic segmentation as the striated branchial and visceral muscles, which arose from the striated muscles of appendages; the endodermal muscles arose therefore from unstriated appendicular muscles.

In this way the whole musculature of the new gut receives a uniform explanation up to the end of the small intestine, and at the same time a similar explanation is given for the differences between the somatic and splanchnic segmentation. As previously mentioned, all new segments formed after the establishment of the vertebrate stage would be somatic segments; owing to the cessation of the formation of appendages no new splanchnic segments would be formed. In the vertebrate body the somatic segmentation both for the unstriped as well as the striated muscles would thus be manifest throughout its whole length; this is clearly the case, for the lateral chain of the sympathetic supplies segmentally motor nerves to the dermal muscles just as the ventral roots supply motor nerves segmentally to the longitudinal muscles of the body. On the other hand the splanchnic segmentation would be confined to the head region of the body,

and so account for the innervation of the endodermal muscles of the whole of the small intestine by nerve cells connected with the vagus nerve.

The innervation of the endodermal muscles of the cloacal region of the gut is so similar to that of the endodermal muscles of the rest of the gut, with the substitution of the connector fibres of the pelvic nerve for those of the vagus nerve, that I am strongly inclined to attribute the formation of the cloacal region to the same kind of agency as has been already argued for the front part of the gut. The difficulty is that there is no evidence here of any lateral root system like that of the bulbar nerves, or of a double segmentation as is implied by the presence of a lateral root; but if, as is most probable, the muscles of the appendages in this sacral region were all unstriped, then, as already argued for the vagus region, the lateral roots to such appendages would have arisen originally from nerve cells in the sacral region of the cord, and when those nerve cells become peripheral, there would be left only their connector nerves remaining—the pelvic nerve—to indicate their original position. On this most probable supposition, that in this region the appendages of the ancestral animal possessed only unstriped muscles, the formation of the cloacal portion of the alimentary canal is in complete harmony with that of the rest of it.

It is not so easy to imagine the genesis of the ectodermal musculature which belongs to the somatic segmentation; it can hardly have arisen from the longitudinal body muscles of the annelid, for although unstriped they resemble the body muscles of Ammocœtes in general structure so closely as to make it most improbable that they have given origin to muscles so different in character as the dermal musculature: indeed it seems to me that the longitudinal body muscles have remained practically unchanged through the annelids, arthropods and vertebrates. There are left the circular muscles and the dorso-ventral somatic muscles; it is possible to conceive their origin from the circular muscle group, but there is no evidence that adrenaline will cause contraction of any member of this group, and the characteristic of the dermal musculature, which they share with the vascular musculature, is their response by contracton to adrenaline or to stimulation of motor nerves belonging to the sympathetic nervous system. This fact suggests that we must look for the origin of

the dermal musculature to the same source as that of the annelidan vascular musculature rather than to circular or longitudinal muscles.

It is perhaps of some significance that the nerves to the vascular muscles in Hirudo leave the nerve trunk in conjunction with the nerves which supply only certain dorso-ventral muscles; this suggests the possibility of a common innervation of these dorso-ventral muscles and the vascular musculatures. If that is the case, then these dorso-ventral muscles ought to contract in the presence of adrenaline. Whether any dorso-ventral muscles in Hirudo contract to adrenaline I cannot yet say. My son has not yet made any experiments to test this action on any dorso-ventral muscles; the muscles which gave no evidence of any such contraction were the longitudinal and circular muscles of Lumbricus. The dorso-ventral muscles of the leech when contracted flatten the animal and are used when it swims through the water; they, like the longitudinal and circular muscles, are paralyzed by curare, and in that respect resemble the voluntary muscles of the vertebrate rather than the involuntary muscles. Still there is the possibility that the dorso-ventral muscles may have assisted in the formation of muscles belonging both to the voluntary and the involuntary nervous system in the vertebrate, and helped therefore to form not only the striated segmental dorso-ventral muscles but also the unstriped ectodermal muscles of the somatic segmentation. If that were so I should expect to find that some dorso-ventral muscles responded to adrenaline and others to curare.

On the other hand, if the dermal muscles arose independently of the vascular muscles, it would be reasonable to find them represented in the lowest vertebrates; but there is no sign of any involuntary musculature under the skin in the Cyclostomes or indeed so far as I know in any fishes, while the vascular musculature is well developed, and both sympathetic cells and chromaffine cells are always to be found.

Whatever conclusion the future may determine as to the relationship between vascular and dermal muscles, it would appear that certain of this group of muscles were involved in the formation of the new alimentary canal, and so formed the sphincters of the gut. It is possible that the dermal musculature assisted in the formation of the original alimentary canal

throughout its whole length, and afterwards became more and more confined to the parts where sphincter muscles were necessary and advantageous.

Lastly, I will consider the origin of the system of muscles derived from those surrounding the segmental duct. The excretory organs of vertebrates are universally considered to have been derived from the segmental excretory organs of annelids, and in the leech these excretory organs connect with the exterior by a duct in each segment. This duct has well-defined muscular walls and possesses in its course an enlargement, the so-called nephridial vesicle or bladder, with contractile walls. It is natural therefore to look upon the segmental duct system of muscles as originating from this group of muscles, and therefore in a separate category from either the endodermal or ectodermal muscles. This might account for the absence of any sign of reciprocal innervation in this muscular group, and its innervation with both motor and inhibitory nerves from cells of the sympathetic system only. In consideration of the marked manner in which this muscular system in the vertebrate responds to adrenaline, I should expect to find these muscles in the leech also respond to adrenaline; that is a question worth investigation. It is possible and indeed probable that the segmental excretory ducts are ectodermal both in the annelid and the vertebrate, in which case this muscular system would belong to the ectodermal system of muscles in both cases.

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INDEX

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