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By
DR. HEINRICH HIGIER
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VEGETATIVE NEUROLOGY

THE ANATOMY, PHYSIOLOGY, PHARMACODYNAMICS AND PATHOLOGY OF THE SYMPATHETIC AND AUTONOMIC NERVOUS SYSTEMS

By

DR. HEINRICH HIGIER
OF WARSAW

AUTHORIZED TRANSLATION BY
WALTER MAX KRAUS, A.M., M.D.
NEW YORK

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CONTENTS

INTRODUCTION v

CHAPTER I.

Comparative Anatomy of the Vegetative System 1

CHAPTER II.

Macroscopic and Microscopic Anatomy of the Vegetative System 4

CHAPTER III.

Embryology of the Vegetative Nervous System 13

CHAPTER IV.

Histology of the Sympathetic Cord and Cranial Ganglia 15

CHAPTER V.

Glands of Internal Secretion or Chromaffin Ganglion Bodies of the Sympathetic Anlage 20

CHAPTER VI.

Physiology of the Vegetative System 22

CHAPTER VII.

Pharmacology and Pharmacodynamics of the Vegetative System 52

CHAPTER VIII.

General Pathology of the Vegetative System 60

CHAPTER IX.

Special Pathology and Clinical Aspect of the Vegetative Nervous System 72

BIBLIOGRAPHY 133

INDEX 143

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INTRODUCTION

Under the terms "animal" or "somatic" nervous system are considered all of those tracts which supply sense organs, or voluntary muscles. On the other hand, all nerve fibers which supply the secretory parts of glands as well as automatically acting organs having a smooth musculature may be considered under the heading "sympathetic," or more generally speaking *vegetative nervous system.* Examples of these latter are the intestines, the genital apparatus, the pupil, the blood vessels, the ducts of glands and the skin.

When the question arises why physicians in general know so little of the anatomy and physiology of the sympathetic system, and value it so lightly, in comparison to the cerebrospinal system, and why the vegetative nerves which supply vegetative organs are so little spoken of in all text-books and systems of medicine, this answer naturally presents itself.[1] That as a rule that branch of medical knowledge which plays a small rôle in clinical medicine is neglected by the majority of physicians. There are, to give a well-known example, large groups of muscles, as for instance the deep muscles in the neck and back, the semispinalis, multifides, and intertransversarii, which, for the same reason, are only known by name, or are entirely unknown to clinicians.

This reason for ignorance is on closer observation not only not justifiable, but also without foundation. True, much mystery surrounds the vegetative nervous system, the reason being that the nervous control of vegetative organs and muscles is partly autonomic, and partly influenced by afferent and efferent connections with the central nervous system, connections which cause a quite different reaction from that of the cerebrospinal system. Injury or transection of the ganglia and peripheral fibers does not cause so intense a reaction as the same interference with the cerebrospinal ganglia and fibers. These are but mild and transitory manifestations of the removal or injury of the connecting links.

The sympathetic plays an enormous rôle in the economy and metabolism of the organism because First: it not only partially supplies the motor and secretory functions of those parts of the body which are *unessential* to the maintenance of life (the extremities),

[1] Notable exception is to be observed in the recently published Diseases of the Nervous System by Jelliffe and White (trans.).

but also regulates organs which are *essential* to life, organs which must not cease functioning for one moment—the heart, lungs, liver, stomach, thyroid, adrenals, sweat glands and blood vessels—and second: its ganglion cells and nerve fibers are widely distributed throughout the entire trunk, and lie through almost the entire extent of the internal and external coverings and organs of the body. The fact that the vegetative system undergoes change in its functional activity at every step is sufficiently shown by the marked manifestations of a physiological nature which every emotion produces, as for example, palpitation, pallor, weeping, incontinence of feces, mydriasis and erection. Pathologically the disturbances are seen in *every infection* and *intoxication,* as for example, goose flesh, tachycardia, blushing, sweating and dry mouth; as well as in such common diseases as tabes with its pupillary inactivity, stenocardia, gastric crises and bladder disturbances.

In spite of this there is scarcely any pathology of the nervous system of the internal organs, any "visceral neurology" in comparison to the much detailed pathology of the peripheral or cerebrospinal nervous system, whose smallest branch has its clinical significance. This on the whole applies as well to pathological anatomy, which has only concerned itself with isolated tumors, and traumatic lesions of the cervical sympathetic and the sympathetic cord, as to therapy which has but little to say outside of a few operative procedures upon the sympathetic in Graves' disease, epilepsy, and glaucoma.

During the last few years scientific interest in the sympathetic and autonomic nervous systems has increased enormously, as the many works of an embryological (Frorup, Kuntz), comparative anatomical and histological (Broek, Jacobsohn, Onuf, Collins, L. Müller), physiological (Gaskell, Langley, Lewandowsky, Bumke, Kreidl, Karplus), pharmacological (Loewi, Falta, Rudinger, Fröhlich, Noorden, Meyer), and clinical nature have shown (Head, Mackenzie, Eppinger, Hess). In these connections the question of the vegetative system will be critically examined. Only the most significant of the large groups of facts at our disposal will be considered. A detailed discussion of this difficult chapter, including the fundamental elements of its physiological and anatomical relations, of which the majority of physicians are ignorant, is justifiable, since the new results of histological investigation and of experimental pharmacology have given an entirely new grouping to the older clinical and pathological material. Nowhere is the comprehension of clinical syndromes and the solution of many important psychological

problems so intimately connected with physiological and pharmacological viewpoints as in the realm of vegetative functions.

Research to-day has opened up, so far as the vegetative system is concerned, a field so wide that its limits are yet hidden in the haziness of the future. Many efforts will have to be made in the future in order to light up this subject in all its extent. The most important aspect of scientific research which has thrown light on the vegetative system is undoubtedly the question of the relation of this to the mind, to metabolism, and to the glands of internal secretion. It has taken but a very short time to accomplish a large amount of work on the subject of the pathology of the vegetative. This work has extended into the most varied branches of medicine, produced a mass of stimulating problems, and has incited the spirit of research to restless endeavors. The nature of the discussed matter, which in many respects is but *in statu nascendi,* leaves little doubt that our résumé must be incomplete, and, especially in the general considerations, can but suggest a few guiding points, special questions, which have particular significance and relation to the practical side of the subject.

For the same reasons, a detailed review of the literature, especially the older literature, must be given, on account of the abundance of facts it contains. The experimental literature, clinical and purely morphological, is the basis of this work. Only its most important aspects will be considered and even these can not be gone into in great detail. A thorough discussion of the history of the subject is without the purpose of this work. Only such special works as will give new and extensive reference to the literature will be mentioned.

Though many things must yet be made clear, there is enough material at hand to permit a fairly precise review of the question of vegetative neurology.

My personal experience with the vegetative nervous system will soon appear in a special article "A Discussion of The Vagus—Sympatheticus Relations."

Owing to the absence of Dr. Krauss, M.C., U. S. A., in the A. E. F. in France, he was unable to make final corrections.

CHAPTER I

Comparative Anatomy of the Vegetative System

The completely developed human nervous system is an end product of a much complicated phylogenetic, and a not less complicated ontogenetic development, extending over a long period of time. As Edinger and v. Monakow, Van der Broek and Froriep have justly observed, it cannot be understood either in its construction or in its functions without a review of the relations existing between the numerous successive phases of its development. Interesting points of view are derivable from embryology and comparative anatomy which help in understanding the progressive development of the function of the vegetative system.

All actions of animals, all movements of the external and internal muscles result from conduction of stimuli of external or internal origin *to* the nervous system.

The various parts of the nervous system which receive these stimuli are designated as the "urhirn" or archeopallium of Edinger. This exists alike in all animals from fish to man, and only varies in size according as one or the other sense is more important for the preservation of life of the particular animal.

All activities in the "urhirn" are reflexes, not only the many mechanisms for movements, but also those for inhibition. These latter make it possible for the animal when subjected to the influence of all kinds of stimuli, to avoid being in continual activity. On the basis of various phylogenetic standards, the central nervous system was regarded merely as an apparatus for seeking and absorbing nourishment; it was stimulated by the sense organs and the nerves of instinct or visceral nerves. The oldest and simplest movements, both exteroceptive and interoceptive, are, in this sense, for the purpose of maintaining life, protecting the body, or guarding against harmful stimuli. The gradually developing new "anlagen" develop at the expense of the old, assuming functions which in lower stages of development were only performed by the old structures, and which in higher stages of development become rudimentary.

One of the earliest organized forms of the "urhirn" of the central nervous system (invertebrates) is that of the loosely connected pairs of ganglia, the ganglion system.

In the lowest vertebrates the so-called metameric system, together

with the "anlage" of the vertebræ, is built up on the ganglion system of invertebrates. This keeps on developing, partly at the expense of the ganglion system. The metameric system develops from more or less similar segments of the spinal canal, each of which has a well-coördinated innervation which supplies the corresponding segment of the body. In every metamere, which has an autonomic central apparatus, there is also a related nervous equipment for the orderly use of the extremity of this metamere. Following this stage of development there is, as in fish, a more extensive differentiation of the brain canal into five brain segments, the telencephalon, diencephalon, mesencephalon, metencephalon, myelencephalon, in which a cortex is as yet entirely lacking, and in which the dominating rôle and sharing of the highest nervous connections belongs to the mid-brain or mesencephalon.

In the next highest vertebrates (reptiles) there is built up upon the now very important mid-brain, what has been designated as the cortico-somatic cerebral system, the new brain or neopallium of Edinger. This is the most important part of the cerebral cortex.

In the lower mammals there remain isolated, relatively independent nervous connections which have been left from the ganglionic, metameric and mid-brain systems.

In the higher mammals, the psychic growth finds its anatomical expression in the addition to the cortico-somatic system of a cortico-associative system with scattered association areas located throughout the much extended and folded surfaces of the cortex. This system, according to v. Monakow, represents in man the preliminary worthy conclusion of phylogenetic development.

In this organization, old and new phylogenetic functional systems work by the side of and with each other in wonderful fashion. This holds not only for visceral and sensory stimuli and for impulses coming from them but also for the corresponding motor impulses. The new brain (neopallium), present at first only in traces, finally comes to equal the "urhirn" or archeopallium in dimension. In monkeys and man, it even surpasses it in size. Thus, as has been stated, the "urhirn" becomes related by fiber systems with a most important apparatus which gives the power to correlate sensations with each other more thoroughly, to retain sensations for some time, to make movements voluntary, and to relegate to the background the reflex and automatic vegetative life. This leaves an animal with more of a "soul" and freed from the continual activity of its reflexes.

What has been said of phylogenetic development holds also for

the ontogenetic, which on the whole is but a much abbreviated recapitulation of the former. Even in the human fetus, it is found that the myelinization rule of Flechsig bears this out. Myelin sheaths develop first in the ganglion system, then in the metameric system, then in the mid-brain system, and finally in the cerebral and cortico-associative systems.

In considering the world of instinct and desire which is so intimately related to the vegetative system, one must conclude, from a biological viewpoint, as v. Monakow has justly done, that all nervous functions have had their phylogenetic origin in the activity of the oldest sense cells and the direct descendants of these cells. Among these must be included the little known paraganglion cells, the chromaffin cells and above all the cells of the sympathetic and autonomic ganglia, *i. e.,* the ganglionic system.

Undoubtedly one finds in the ganglion system of quite low animals a well-defined localization in the sense that the various viscera, glands, excretory and sex organs, as well as the circulatory and respiration apparatus, etc., have a separate and delicately constructed representation.

The ganglion system which in higher animals retains the lowly rôle of serving the vegetative nervous functions, successively obtains a second representation in the metameric system, the spinal cord, a third in the brain stem (central gray matter, mid-brain and probably in the corpora quadrigemina and optic thalamus), and finally a fourth, which is double, in the cerebral cortex. This is a quite diffuse and spatially narrowly bounded, possibly strictly focal area of cerebral surface, lying near the cortical orientation system or the cortico-somatic system which serves the purpose of innervating individual vegetative organs.

Finally, since cortical localization of vegetative functions in the brain is to be discussed more fully below, we may say that as far as we know *definitely,* the cortex of the cerebrum only serves conscious perception (Gnosia), conscious action (Praxis), and the thought innervations necessary to these.

CHAPTER II

Macroscopic and Microscopic Anatomy of the Vegetative System

What may be learned from the macroscopic anatomy of the sympathetic, which not only is the Alpha and Omega of the visceral system, but also the bearer of the burden of the mechanical work of our vegetative life?

Two parts may be distinguished: the cord and the branches.

The cord, usually spoken of as the sympathetic cord, is divided into three parts—cervical, thoracic and abdominal.

The branches also are divided into three parts—those to arteries, those to the periphery, and the communicating branches.

The fact that the sympathetic cord is a symmetrical organ, lying immediately in front of the vertebræ and parallel to it must not be overlooked. Its extent is from the base of the skull to the coccyx. It is extrapleural and extraperitoneal, and ends at its lower end in a loop, a thread or an unpaired ganglion. In lower animals, as fish, which preserve their segmental structure to a marked degree, the sympathetic cord has a ganglion at the level of each vertebra, giving it the appearance of a string of pearls. Every sympathetic ganglion lies, in the majority of cases, either on the vertebra, or on the costal process, and for that reason is called a *sympathetic or vertebral ganglion.* This is in contrast to the spinal ganglia, belonging to the cerebrospinal system, which are associated with the posterior sensory root and are, on account of their anatomic position in the intervertebral space, called *spinal or intervertebral ganglia.*

The ganglion system described in the section on comparative anatomy is most conspicuously seen in the thoracic and upper lumbar regions where the segmental structure of lower animals is preserved more than in any other place. Thus, the twelve thoracic vertebra ribs have twelve corresponding ganglia.

In the cervical and lumbar regions, where the embryonic arrangement is lost, the ganglia fuse, a fact which may be seen by their mulberry-like form.

Thus it is found that in the neck there are fused growths of ganglia, superior, middle and inferior ganglia, while in the lumbar region several of the ganglia are incomplete and insignificant-looking.

So much for the sympathetic cord, its vertebral ganglia, and their relation to the spinal ganglia of the spinal cord.

In regard to the branches, the following is the usual classification:

I. Arterial branches or vascular plexi.

(*a*) Cranial or carotid plexus. This begins at the upper cervical ganglion, and passes cranialwards, surrounding the carotid arteries. It supplies the cranial cavity with sympathetic fibers.

(*b*) Thoracico-aortic plexus. This supplies the heart, aorta, lungs and esophagus.

(*c*) Aortico-abdominal plexus. This encircles the three large unpaired branches and supplies the abdominal viscera and the mesentery with fibers.

Other smaller plexi are the laryngeal, thyroid, cardiac, pulmonary, esophageal, celiac, mesenteric, renal, spermatic, hypogastric, uterine, vesical and cavernous.

II. Peripheral branches connect with the important cardiac branches of the abdominal cavity. The cardiac branches are given off from the third cervical ganglion and from the cardiac plexus. The splanchnic branches are given off from the lower six thoracic ganglia and go from the thoracic to the abdominal cavity, where they supply the gastro-intestinal tract and its appendages.

III. Communicating branches connect the sympathetic ganglia with the anterior spinal roots. This makes an important connecting path between the sympathetic and central nervous systems.

In the make up of the sympathetic, the third part of the central nervous system, there are to be found other large structures of obscure nature, as paraganglia, chromaffinic glandular structures and the prevertebral celiac, cardiac and stellate ganglia. Of these more will be said below.

What has been said thus far includes the main points of import in the gross anatomy of the human sympathetic system.

It now becomes a question of accounting for the close relations of the sympathetic to vascular and spinal structures. What is the significance of the sympathetic cord? Is it a special single nerve, or a conglomeration of various nerves? What purpose do the sympathetic plexi, and the large thoracic and abdominal ganglia lying next the vertebral ganglia serve? What is the relation of the rami communicantes to the sympathetic cord on the one hand, and to the spinal cord on the other? These are the main questions which we wish to try to answer on pure anatomical bases.

The dorsal spinal cord, and the near-by sympathetic will serve as a paradigm for the explanation of these important questions. These

sections have retained more than any others the metameric type, as revealed by comparative anatomical and embryological studies. They offer opportunities to study the characteristics of the vegetative system from a morphological point of view, thus leaving out the necessity of using the evidence to be gained by delicate biologico-chemical reagents. These latter reactions will be considered later. The metameric type of structure is entirely lacking in the cranial part of the vegetative, while in the cervical and sacral parts it is, as has been said before, but poorly developed.

In long past epochs, as phylogeny teaches, the "urhirn" alone played the rôle of ruling functions controlled by the nervous system. Each segment of the nervous system probably had its own separate spinal and sympathetic nerves, each metamere was autonomous, and had little to do with its neighbors. The somatic regions of a segment included the ganglion cells of the spinal cord which subserved the function of transmitting the impulses to and from voluntary muscles, and of receiving impulses from the overlying skin. The vegetative regions supplied the automatically acting involuntary muscles with motor nerves, and the organs of its own segment with sensory nerves. Visceral receptor nerves are found not only in mucous membranes, which are normally considered sensitive to stimuli, but also in all the tissues and organs, as the liver, lungs, blood vessels and kidneys. The receptors for this part of visceral innervation probably pass in the paths from the spinal ganglion cells, and go thence to the central system via spinal ganglia.

The central origin in the spinal cord of the vegetative tracts is most probably in Clarke's columns, and in the lateral segments of the gray matter (the lateral horn of the spinal cord). From there, the nerve fibers pass out via the anterior roots as thin, white and medullated, centrifugal fiber bundles (ramus communicans albus s. efferens). They pass to the vertebral ganglia (see Fig. 1).

The fibers are always interrupted in a ganglion, the so-called "synapse." They then leave the ganglion cells as another gray, motor, unmedullated fiber bundle (ramus communicans griseus s. afferens). They are centrifugal, but never centripetal. These go uninterrupted to the peripheral vegetative end organ, be it the pupil, heart, lung, stomach, sweat glands, hair muscle or vascular muscle.

The white rami branch off in the ganglia of the sympathetic cord in such a way as to yield three to five branches which entwine themselves about a corresponding number of ganglia (Langley, Onodi). Every ganglion cell of the sympathetic cord has but one axis cylinder. This, as a gray fiber, proceeds to the periphery (Van Gehuchten).

The communicating tracts there are divided in their course into a white and gray branch, or more generally speaking, into a pre- and post-ganglionic part. As a rule the white rami go from the spinal cord to the sympathetic cord, and the gray rami go from the sympathetic cord to the viscera, or via the spinal nerves of the end organs at the periphery.

In a cross-section of a metamere, the following is found:

1. The spinal anterior horn with its motor root for the innervation of voluntary muscle.

2. The spinal posterior sensory horn and the neighboring trophicosensory spinal ganglion for the reception of internal and external, interoceptive and exteroceptive stimuli.

2. The vegetative spinal lateral horn with a ramus communicans albus, a sympathetic ganglion and a ramus communicans griseus. These are intended for glandular and hollow muscular internal organs (visceral fibers), and for the end organs of the skin (pilomotor, secretory and vasomotor fibers).

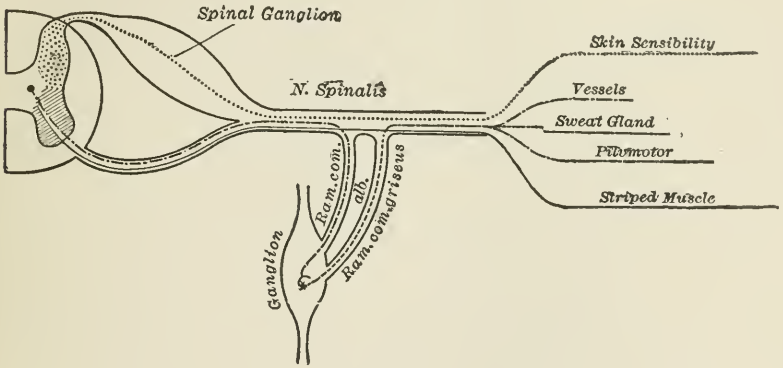


FIG. 1

Stimulation of the sympathetic nerves is usually not perceived in consciousness (normal failure of sensations from vegetative end organs) but it increases the tone and activates the nerves innervating smooth muscle.

An attempt will now be made to identify the three metameric divisions in other regions, including the vegetative system where the regular metameric structure is found in modified form, or is entirely lost. The following, partly developmental, partly anatomic considerations, show that the original structure is lost and that many new structures have appeared.

(*a*) The unequal distribution and inconstant position of the ver-

tebral ganglia or synapses in which the interruption of the sympathetic fibers takes place, causing the spino-peripheral sympathetic fibers to be divided into two parts.

(*b*) The inconstancy of the rami communicantes in contrast to the regularity and constancy of the intervertebral ganglia.

(*c*) The unequal distribution of the important sympathetic centers in the cerebrospinal gray matter.

(*d*) The incongruity between embryonic metameres and later cranial and spinal segments.

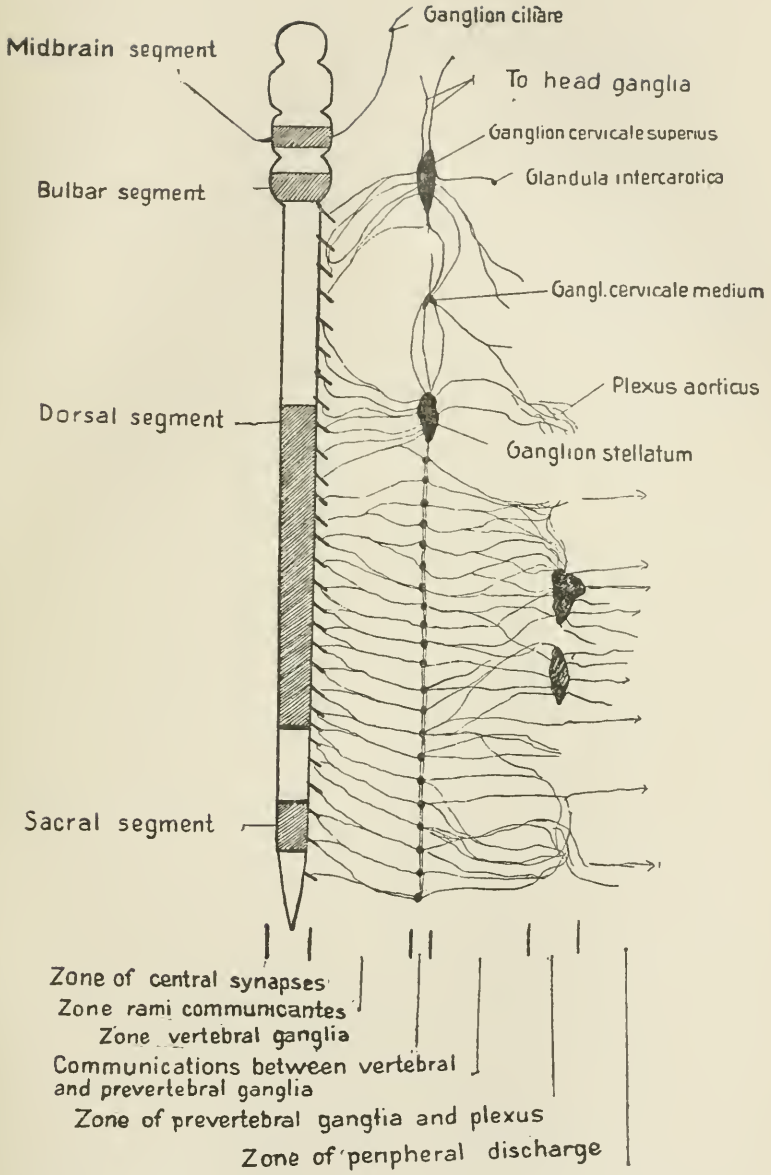
These four questions will be briefly considered theoretically and practically. (For pictorial representations see Fig. 1 and Table I.)

I. *The Unequal Distribution and Inconstant Position of the So-called Synapses.*—Every communicating branch, after leaving the spinal cord, is interrupted in a ganglion cell of the sympathetic, and thus forms two neurones, in contrast to the single neurone of the somatic nervous system. But all medullated sympathetic fibers are not interrupted in the sympathetic cord. Many fibers go through the ganglia undisturbed to proceed upward and downward to the next ganglion where the medullary sheath is lost and the fiber is interrupted, becoming post-ganglionic. In this way, even the sympathetic cord becomes a path for white sympathetic fibers.

The sympathetic nerve or ganglia, the N. internodius, which joins the vertebral sympathetic, has like these latter a connective tissue sheath of Schwann. A cross section of this nerve is not like that of an ordinary nerve but contains both sheathed and unsheathed fibers as well as ganglion cells. Therefore the N. internodius is not a nerve in the ordinary sense, but a much extended ganglion, with white rami communicantes included. This applies both to the cervical and abdominal sympathetic cord (N. splanchinus), both of which represent a union of many white rami communicantes into large nerve bundles. The sympathetic cord is, therefore, a morphological but not a functional entity.

Many fibers destined to supply the viscera, after taking the above described course in the sympathetic cord, proceed to groups of ganglion cells in the body cavities. Examples of such fibers are those to the heart and uterus. An example of the ganglion cell groups is the celiac plexus with its semilunar ganglion. Ganglia of this type have been designated prevertebral ganglia by Langley and may be differentiated from the above described vertebral ganglia by the fact that they only supply viscera and that their post-cellular fibers never connect with spinal nerves.

The sympathetic plexus, of later phylogenetic origin, may be



Scheme of the Vegetative Nervous System. (After Veraguth.)

regarded as conglomerations of pre- and post-cellular fibers. From this point of view we must regard the carotid plexus which accompanies the carotid artery to the cranial cavity as a conglomeration of fine post-cellular fibers which proceed cranialward from the cervical sympathetic. Prevertebral ganglia are to be differentiated from the vertebral ganglia only by their position. They receive preganglionic medullated fibers, and give rise to post-ganglionic gray fibers, just as do the vertebral ganglia. Many ganglia, as the superior cervical ganglia which supply both viscera and skin glands, are to be regarded as a combined type of vertebral and prevertebral ganglia.

But it must be added that all fibers do not end in the prevertebral ganglia. Many go distalward, uninterrupted, to reach the immediate vicinity of their end-organs and are there interrupted, the white fibers becoming the gray. These ganglia are called peripheral or terminal ganglia.[1] They exist in connection with such organs as the heart, intestines and salivary glands. Many fibers even pass through three ganglia on their way to their end organs. Thus, for example, the white dilator fibers of the pupil arise in Budge's cilio-spinal center, proceed as white rami communicantes through the stellate ganglion and enter the superior cervical ganglion. Here they are interrupted and become gray rami communicantes, going to the pupil.

Since the ganglionic interruptions, the synapses, do not occur at typical localities, but are found not only in the sympathetic cord, but also in prevertebral and peripheral ganglia, it has become the custom to follow the classification of Langley in regard to the topography of these structures. He divides the ganglia into three orders, vertebral, prevertebral and peripheral.

II. *Inconstancy of the Rami Communicantes.*—In man, not every spinal segment gives rise to a communicating branch. Thus, for example, the cervical part of the spinal cord, corresponding to eight metameres, gives rise to none or only isolated white rami. This region has but three cervical ganglia, the superior, middle and inferior. The superior ganglion receives its precellular, partly longitudinal, intraspinal fibers from the upper dorsal segments. Many other sympathetic ganglia as well receive fibers from several (5–6) lower segments (Langley). On the other hand, the sacral sympathetic gets its white rami not only from the mid dorsal and lumbar roots, but also from higher segments (Gaskell). In man, no white rami are given off below the third lumbar nerves. Hence, as may be seen on Table

[1] They are autonomic ganglia, not sympathetic. See section 17, Chap. IV, p. 30 (Trans.), and plate VIII.

I, the cervical and sacral sympathetic are to be regarded as undoubted collected white rami communicantes.

On the other hand, according to Gaskell, the post-cellular gray rami springing from the ganglia join the nearest spinal nerves. These carry fibers for the most part to blood vessels, glands and muscles of the skin. This occurs even in the sacral and cervical sympathetic portions of the sympathetic, though they do not have white rami from their corresponding spinal cord segments.

III. *Unequal Distribution of the Vegetative Centers in the Gray Cerebrospinal Axis.*—The vegetative-automatic centers are not equally distributed in the posterior segments of the gray matter of the region from the mid-brain to the sacral part of the spinal cord. They lie compactly in various regions from which the customary topographical designations are derived. These centers of origin are mesencephalic, bulbar, dorso-lumbar (from the seventh cervical to the third lumbar segment) and the sacral (from the second to the fourth sacral segment). This is not meant to give the impression that the remaining parts of the cerebro-spinal axis do not contain centers for automatically acting organs, but that they are probably there, either rudimentary in man or occupying but very little space.[2]

IV. *Incongruity of the Embryonic Metameres with the Later Cranial and Spinal Segments.*—Every ganglionic segment supplies nerve fibers to that part of the body which represents its ontogenetic and embryonic metamere, not to that part which corresponds to it in life (post-fetal stage). This is the cause of the enormous shifting and apparent variations from the fundamental type.

But a few examples of this will be given, examples which in discussing the sensibility of the sympathetic system will be found to be of very great practical importance.

For example, the testicle descends from the renal region into the scrotum, which leads to the apparently incongruous fact that the scrotum and the testicle, which seem to be derived from the same body segments, are supplied one from the lower sacral nerves, the other from the upper lumbar nerves. This accounts for testicular pain in nephrolithiasis and for increased irritability of the external genitals and irritability of the testicle in conus and caudal lesions.

The phrenic nerve arises from the spinal cord in common with the fourth cervical nerve. It supplies, among other things, the dia-

[2] Probably due to the fact that the segments not having vegetative centers are mainly concerned with the innervation of the extremities, *i. e.*, the cervical and lumbo-sacral enlargements. (Trans.)

phragm and the liver, thus accounting for pains in the arm in cholelithiasis and diaphragmatic pleurisy.

Following the development of the upper extremities which are placed between the second and third ribs, we find that the second rib is supplied by the four lower cervical nerves, while the third is supplied by two thoracic nerves (this accounts for pain in the upper arm in stenocardia).

The urinary bladder is supplied by the upper lumbar nerves in that part which is developed from the allantois, while its lower part, developed from the cloaca, is supplied by the middle sacral nerves.

In considering organs which are vegetative in function par excellence, the vagus takes a prominent place, since this nerve arising in the medulla, that is a cranial nerve, supplies all of the thoracic and most of the abdominal viscera. This happens because the nerve in the lower animals from which man has developed extended far caudalward, and because these organs, though far distant from the origin of the nerve, lay closer to the head in these animals. This applies particularly to the heart, lungs and stomach. As a matter of fact, the apparently irregular location of the three vagal nuclei in the medulla is in reality quite like that of the corresponding motor sensory and vegetative centers in the cord, when it is recalled that the nucleus ambiguus is motor, the nucleus solitarius, sensory, and the dorsalis, visceral, and that the medulla is but a continuation of the spinal cord with this difference, that the central canal is widened into the fourth ventricle and the posterior columns and posterior horns are pushed lateralwards.

As is well known, the somato-motor vagus nucleus supplies the voluntary muscles of the pharynx and larynx, the somato-sensory nucleus the meninges, and the mucous membranes of the external auditory canal, the larynx and bronchi, the visceral nucleus, the heart, lungs, stomach, liver, pancreas and upper parts of the intestines.

What we find of practical value from the morphology of the vegetative system, when we consider the descensus splanchnicus (developmental progress caudalward of organs) as an example, is that the rami communicantes of the visceral vagal nucleus, from which arise the autonomic fibers for the intestine, after passing through the synapse of the jugular ganglion near the base of the skull (corresponding to a sympathetic vertebral ganglion), travel from one half to one third the length of the body to reach the peripheral ganglion cells in its end organs.

After this rather lengthy departure from the main plan of this

chapter, we shall now return to the subject in hand and give a brief recapitulation of the anatomic relations of the most important ganglia of the body.

The uppermost ganglion of the sympathetic cord, the superior cervical ganglion or first sympathetic ganglion, receives its pre-cellular fibers from the last cervical segment (C 8) and the upper dorsal segments (D 1–3). These supply the skin glands, blood vessels and pilomotor muscles of the head as well as the dilator pupillæ muscle and Müller's flat orbital muscle.

The inferior cervical ganglion and the stellate or first thoracic ganglion supply accelerator nerves to the heart and most probably vaso-constrictor fibers to the pulmonary vessels. The preganglionic fibers arise from D 1–5.

The largest ganglion of the abdominal cavity, the celiac, gives off the most important branches in the celiac plexus, the major and minor splanchnic nerves. The first is made up of fibers from the fourth to the ninth dorsal ganglion, the latter from the tenth to the twelfth ganglia. They all leave the thoracic cavity by an aperture in the diaphragm and go to the celiac ganglion as precellular fibers. From there, they go as the mesenteric nerves to supply the stomach glands, liver, pancreas, spleen, kidneys, adrenals, and intestines (as far as the descending colon).

The inferior mesenteric ganglion receives precellular fibers from the upper lumbar cord (L 1–3) and sends its unsheathed post-ganglionic fibers to the colon and via the hypogastric nerves to the anus, bladder, vesical sphincter and genitals.

Furthermore mention must be made of the fact that the middle part of the dorso-lumbar sympathetic cord sends fibers to end organs in the skin, the blood vessels of skeletal muscles and of all the viscera between the mouth and rectum.[3]

[3] For a description of the autonomic ganglia and their connections. See section 21, Chap. VI, p. 34. (Trans.)

CHAPTER III

Embryology of the Vegetative Nervous System

The discussion of the development of the vegetative nervous system of vertebrates, and of man in particular, is not by any means closed.

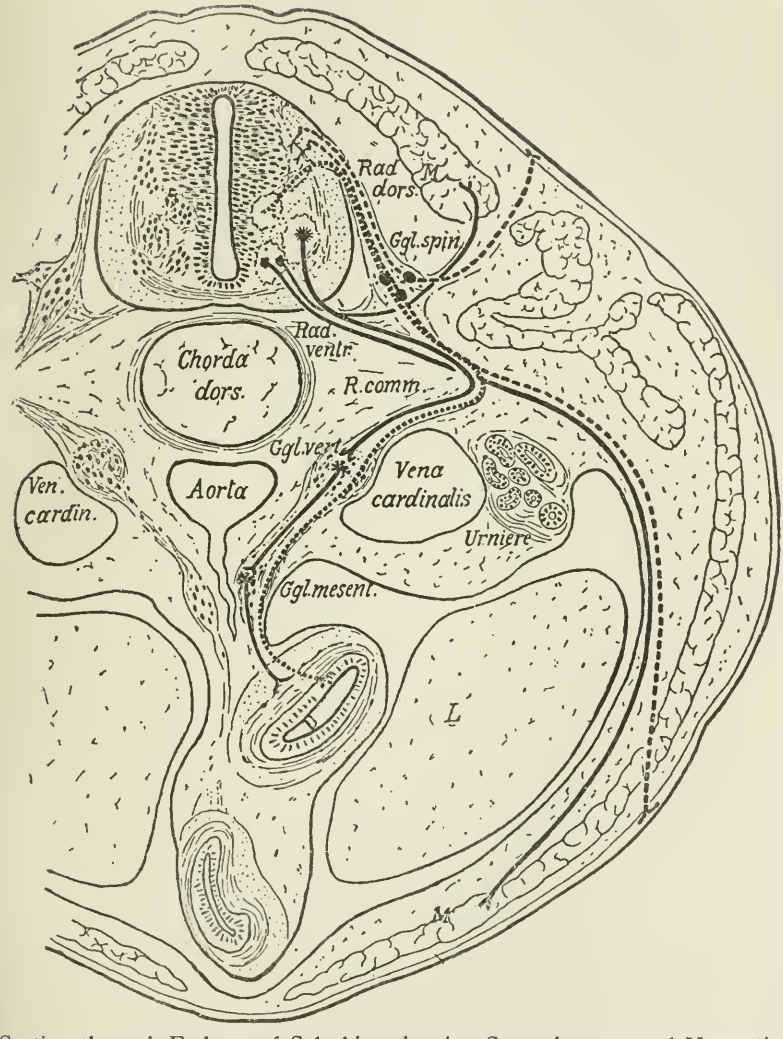
According to the newest investigations of A. Cohn, Kuntz and particularly Froriep, the sympathetic cord develops in vertebrates from a pair of cell columns which lie dorsal and next to the aorta. In earlier stages, cells wander from the ventral half of the neural canal. They leave it in company with the ventral nerve roots as indifferently constructed primitive cells, with large nuclei. They join the main branch of ventral nerve roots. The means by which these cell fibers are carried to the periphery are the neuroblastic branches which grow from the medullary canal towards the periphery, and probably also those fibers which later become the preganglionic fibers of the autonomic system. It is these relatively coarse protoplasmic threads which combine with those of the primitive cells. The cell processes then curve medially as from the spinal curve stem towards the dorso-lateral wall aorta. Near them a group piles up to make the vertebral ganglia. Other cells go further. They go centralwards, combined with protoplasmic threads which lie in the region which exists between the aorta and vena cardinalis. These make the pre-vertebral, and further out the peripheral ganglia.

According to Kuntz, the prevertebral plexus arises in a group of cells which lies ventral to the aorta in the posterior part of the body, while the cardiac and gastro-intestinal ganglia arise from groups of cells which come in from the midbrain and vagus ganglia. One may justly conclude that the excitatory neurones arise in cells which have wandered from the motor roots, while the sensory neurones are derived from the posterior roots. There exists, consequently, a broad analogy between the sympathetic system and the central nervous system. The sympathetic system is but the part of the central system which has functions corresponding to its part.

According to Froriep, the movement of cells to their later places is neither a free wandering [His' Keimcells] or a pure mitotic splitting [Kohn's theory of syncytiate or neurocytial construction of the

sympathetic cord] but a combination of both processes, dependent upon the established paths of the outgrowing neuroblastic ramifications.

These latter come exclusively from the central organs where the corresponding neuroblasts occupy the dorso-lateral zone of the spinal and bulbar anterior horn region.



Section through Embryo of Selachien showing Sensori-motor and Vegetative Arcs. (Froriep.)

CHAPTER IV

Histology of the Sympathetic Cord and Cranial Ganglia

Histologically the vegetative system is characterized by several peculiarities which may be of diagnostic value in differentiating it from other parts of the nervous system. The vegetative differs both microscopically and macroscopically from other parts of the nervous system. The ganglia have a connective tissue sheath and its nerve fibers are sheathless, gray axis cylinders. Their color is due to the absence of the very refractible, whitish myelin.

The vegetative ganglia are very hard to demonstrate in man both microscopically and macroscopically. This is due most probably to the fact that the ganglionic nodes lie very close to tissues which are readily fermented and destroyed after death, such as the nasal mucous membrane, the buccal cavity and the intestinal canal. Being very poorly protected, unlike central nervous system structures, they are easily destroyed.

Ordinary staining methods give the same picture in both spinal cord and sympathetic ganglia—round, processless, protoplasmic bodies with nuclear substance and a nucleolus surrounded by a capsule,—a fibrillary tissue. On more careful examination, even with this unreliable staining method, it has been shown (L. Müller) that the cells of the spinal ganglia are larger, have a more conspicuous capsule and more nuclear material than those of the sympathetic ganglia. More delicate staining methods (impregnation with metals) (Ramon y Cajal, Bielschowsky) or vital methylene blue staining (Ehrlich) show that the fundamental difference exists between the cells of the spinal ganglia and the sympathetic cord. The former are decidedly larger, uniformly oval or round and have but one process. This process is a uniformly broad band which either encircles the cell or forms a corkscrew-like figure; the latter—the sympathetic cells—are mostly of a multipolar nature, have many dendrites and always have a nucleus and a nucleolus.

There are great differences in the structure of the cells, in their axis cylinders and the size of the dendrils, corresponding to variations in location and function.

Further details about the various structure of cranial ganglia, vertebral, prevertebral and organ ganglia cannot be given here. This

much may be said, however: L. Müller has differentiated the main types of sympathetic ganglion cells; those of the sympathetic chain, the solar and semilunar ganglia, the ganglion of Wrisberg and the ganglion bulbi aortæ on one hand, those of the remaining ganglia on the other. Classifications may be made; those with extra and intracapsular processes, with thin or thick dendrites, with short and long, ramifying or forked dendrites (crown cell type) with thick or thin capsule (Klein, Cajal, Dogiel, Michailow).

Histological examination has also shown that groups of ganglion cells do not always form ganglia. Furthermore, they are scattered through nerve trunks without causing any swelling in them which could be identified with the naked eye as a ganglion. Examples are the submaxillary and Wrisberg's ganglia.

The axis cylinder is readily differentiated from the dendrites by its width and its fibrillary structure.

The old teaching of Gaskell and Langley that the nerves of the vegetative nervous system which are precellular or preganglionic are sheathed, while the postcellular or postganglionic fibers are unsheathed, is still accepted generally. Yet there are exceptions to this rule as the postcellular fibers going to the intestines via the mesentery, the precellular fibers in the ciliary nerves and many others.[1]

The origin of the vegetative tracts in the spinal cord are readily recognized. The nucleus lateralis or sympatheticus may be recognized in the dorsal part of the lateral horn of the grey matter by the size and form of the cells. These are smaller than the multipolar cells of the anterior horn, are round, or pear-shaped, occasionally spindle-shaped, club-shaped or spermatozoa-shaped and seem to have no processes on low magnification. (Paracentral cells. Jacobsohn.)

The vegetative paths in the medulla arise in similar cells of the formatio reticularis.

The anterior and posterior spinal root join to form the short spinal nerve (Fig. 1). The white rami communicantes are supposed to arise from the posterior roots.

The small sheathed fibers undoubtedly come from the anterior roots. The sympathetic fibers leaving the spinal cord are smaller than motor fibers. The former measure about 3μ (see text), the latter 16μ.

The visceral fibers are readily recognized in the mixed motor bulbar nerves (N. Vagus) and in the motor roots. The former have a thin sheath. The latter (visceral fibers) (motor fibers) a thick one. Embryology shows that the former are myelinized later

[1] See W. H. Gaskell, The Involuntary Nervous System. Chap. IV, p. 65. (Trans.)

than the former. The white rami go to that sympathetic ganglia in which the first neurone ends. Here it comes in contact with the second postcellular neurone. From thence it becomes a grey, sheathless fiber.

It is worth noting that the white ramus, which goes as a 1 cm. long fiber to the ganglion, usually lies in the same nerve bundle as the grey ramus. These latter return to the spinal nerve and proceed peripheralward. For this reason, it is not always easy to differentiate between the white and grey rami.

Precise observations concerning the spinal centers of the sympathetic centers, we owe to English authors, most prominent among which are Langley, Sherrington, Gaskell, Onuf and Collins. Recently Jacobsohn has gone over the old work by examining a complete set of serial sections from a human spinal cord stained by the Nissl method. According to Jacobsohn, there are two columns of vegetative cells.

(I) The lateral cell-column is composed of two parts: (*a*) An upper column corresponding to Langley's "Sympathetic System." This lies in the lateral horn of the dorso-lumbar cord ($C_8 — L_3$) and is designated the Nucleus sympatheticus lateralis superior s. cornu laterale. (*b*) A lower column lying in the sacral cord, from S_2 caudalward. It is placed between the anterior and posterior horns and is designated the Nucleus sympathicus lateralis inferior s. sacralis.

The dorsolumbar column is thickest at the upper dorsal segments and at the upper lumbar segments, that is near the cervical and lumbar enlargements where there are collections of ganglion cells for the extremities.

(II) The medial cell column lies in the medio-ventral marginal zone of the anterior horn of the lumbosacral cord, from L_4 distalward and is designated the Nucleus sympathicus medialis s. lumbosacralis. Low down in conjunction with the Nucleus radialis, it forms an area of groups of cells which takes up almost the entire anterior horn and the space between.

All the cells of these three columns have the following three characteristics: (1) They are always in groups and closely packed together. (2) They are long, round, club-shaped or vesicular, rather small, round cells. (3) They have a homogeneous appearance and are usually stained more darkly than the larger, less closely packed motor and sensory cells.

Microscopic investigations have established the fact that the above described type of cell found in the ganglia of the thoracic

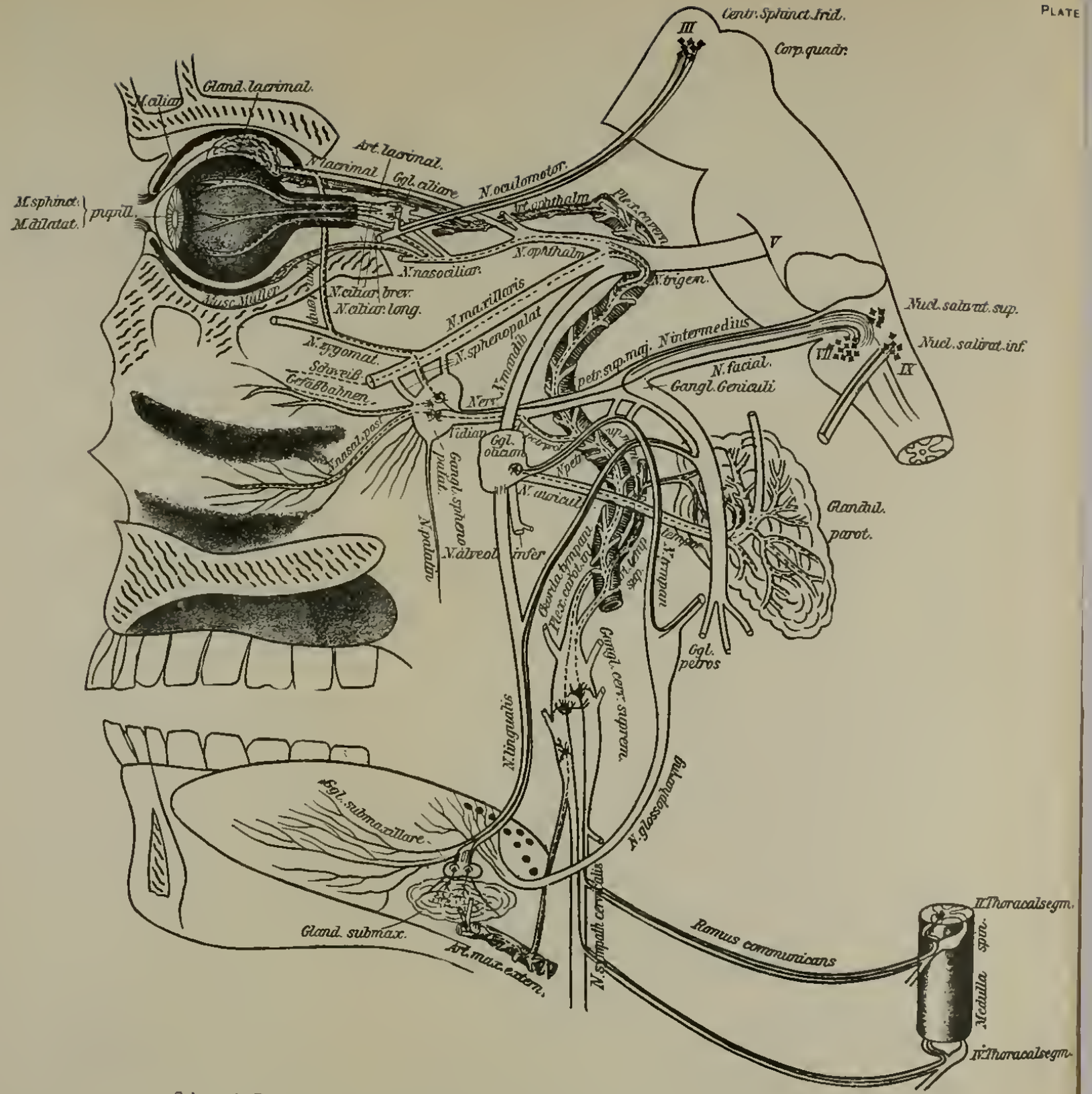
metameres are also demonstrable in the cranial structures. These represent a conglomeration of several metameric segments in which the position of the intervertebral spaces, sympathetic tracts, spinal and sympathetic ganglia are considerably modified. It has been shown that many of the cerebral ganglia are analogous to a modified spinal ganglion. Examples are the geniculate and Gasserian ganglia. Others are mixed ganglia resulting from the merging of the sympathetic and spinal ganglia. An example is the jugular vagus ganglion. A third group includes the pure vertebral or vegetative ganglia, the ciliary, otic, sphenopalatinum, submaxillary and sublingual. The fibers for blood vessels, the smooth muscles of the eye, and the tear, salivary and mucous glands pass through this last group of ganglia.

If we start with a cross-section of the medulla, that is, that plane of the cerebrospinal axis in which the most important cranial nerves are placed, we find, in addition to the large multipolar motor cells, small circumscribed groups of oval or pear-shaped unipolar cells (paracentral cells). These are the nuclei from which the preganglionic rami communicantes spring. The nuclei are as follows (Plate 3):

(1) Nucleus pupillaris (Bernheimer)—median to the oculomotor nucleus.
(2) Nucleus lacrimalis—median to the facial nucleus.
(3) Nucleus salivatorius superior (Kohnstamm)—dorsal to the facial nucleus.
(4) Nucleus salivatorius inferior (Kohnstamm)—near the glossopharyngeal nucleus.
(5) Nucleus dorsalis vagi—between the motor and sensory vagus nuclei, i. e., between the nucleus ambiguus and the nucleus solitarius vagi.

A closer analysis of the anatomical position of the various vegetative nuclei shows that their relation to sensory and motor nerves is the same as in the spinal cord.

As a paradigm we shall take the most orally placed ganglion—the ciliary. It is of great clinical significance. For years well known authors have spoken of this ganglion as a spinal ganglion or a mixed ganglion (Schwalbe, Budge, Remak, His, Gehuchten, Kölliker, Bach). A cross-section of the brain stem shows the following: the oculomotor nerve is the anterior motor root, the trigeminal nerve is the posterior sensory nerve, the Gasserian ganglion corresponding to a spinal ganglion while the ciliary ganglion is the vegetative ganglion.



Schematic Representation of the Vegetative Nerve Innervation of the Head. (Muller & Dahl.)

The white rami go from the visceral nuclei via their corresponding motor nerves. L. Müller and Dahl have tried to establish this on a firm basis.

Afferent and efferent may be differentiated in the cranial ganglia as well as in those of the sympathetic chain. The white rami communicantes pass via the anterior motor roots in the cranial as well as in the spinal region. Many rami albi spring from cranial nerves and have been anatomically described though the part they play was not even thought of. (Plate III.)

(1) Radix motorica, or R. albus ganglii ciliaris—from the oculomotor.
(2) Nervus petrosus superficialis major, or R. albus ganglii sphenopalatini—from the facial.
(3) Nervus tympanicus and its process going to the otic ganglion—nervus petrosus superficialis minor, or R. albus ganglii otici—from the motor part of the glossopharyngeal nerve.
(4) The chorda tympani, which sends fibers as the R. albus to the submaxillary ganglion—from the motor nervus intermedius.

The post-cellular tracts of the cranial ganglia are like those of the sympathetic chain, sheathless. They supply smooth muscle and glands exclusively. When they have a long path to follow to reach the organs which they innervate, they join sensory nerves. The reason that the vegetative fibers, when they do not form separate nerves, join sensory nerves and not motor nerves, is no doubt that sensory nerves are more widely distributed and go to all tissues.

CHAPTER V

Glands of Internal Secretion or Chromaffin Ganglion Bodies of the Sympathetic Anlage

Many authors include in the sympathetic system various glands which contain chromaffin cells, that is to say cells which have a great affinity to chromium, and on that account take up an intense brown coloration in Müller potassium bichromate solution. These cells all develop from the sympathetic anlage, and are therefore in very close relationship to the ganglion cells. They are found partly separate, partly in small groups in the sympathetic system, in the sympathetic ganglia, or in large nerve networks about blood vessels. Where they are found as individual bodies they are designated PARAGANGLIA.

They are for the most part spherical with a connective tissue capsule and are broken up by large nerves and blood vessels, between which the chromaffin cells lie in unequal masses.

Of the larger chromaffin bodies the following four may be named: (1) the carotid paraganglion incorrectly spoken of as a gland [carotid gland or epithelial organ]. (2) The coccygeal paraganglion incorrectly spoken of as the sacral gland [coccygeal gland]. (3) Aortic paraganglion at the bifurcation of the aorta. (4) The best studied and largest chromaffin body, the suprarenal body, the medulla of the adrenals, from which the active blood pressure raising adrenalin is produced, a substance which stimulates the sympathetic system, and plays an enormously important rôle in the body.

According to Aschoff, chromaffin bodies are also to be found in the vicinity of or in the paroophoron and epididymis which are also organs of internal secretion.

The chromaffin, or more properly speaking phäochrom cells [Poll] all develop from the sympathetic anlage, and are at least closely related to the ganglion cells. The assumed transitions between the two have not received general confirmation, and, in spite of the hypothesis of Diarnera that the chromaffin cells are secretory epithelial cells, H. Kohn, one of the first describers of this picture, justly maintains the propriety of not putting these cells in any definite histological group but in a group of their own.

These cells, which may resemble alike epithelial cells, muscle cells, and nerve cells, also take their place, both embryologically and physiologically as a distinct type very closely related to the sympathetic cord.

CHAPTER VI

Physiology of the Vegetative System

What are the physiological characteristics of the vegetative nervous system? The proof of even the most simple of these is more or less difficult to obtain since, with the exception of the cervical sympathetic, the structures are very inaccessible. The retro-pleural and retro-peritoneal ganglion nodes and nerve borders are so hard to get at that transection, stimulation or extirpation on the living animal can hardly be done. In reviewing the separated functions of the vegetative system, localized in the cerebral cortex (neopallium), the cerebrospinal axis (archæopallium), the ganglia and the periphery respectively, we find the following:

1. *Autonomy of the Peripheral Vegetative System.*—There is a distinct autonomy and independence of the periphery. For example, the progress of digestion is possible without the influence of the cerebrospinal axis as experienced in the simultaneous transection in dogs of the spinal cord and vagus nerve. Animals in whom a part of the spinal cord, or even the entire brain, has been removed, live without them, digesting, voiding and developing. The independence of the periphery is anatomically proven by the fact that smooth muscle does not degenerate after its nerves are cut. It is as yet undecided whether, since the end organ can functionate independently, there are ganglion cells in its walls as in the blood vessels, or whether the autonomy resides in the protoplasm of the organs themselves. It is noteworthy that many organs have no ganglion cells in their walls and that the embryonic heart muscle contracts rhythmically for a time even though it has no ganglion cells. The physiological relations are therefore quite different than in the cerebrospinal system, in which permanent and severe changes occur in circumscribed disease of the brain and interruption of conduction bundles. In lesions of the sympathetic ganglia or their peripheral branches, there is at most a transitory disturbance of function in the corresponding organ. In many cases it is demonstrable that after the cerebrospinal axis has been cut off there is complete paralysis; *e. g.,* in intrinsic muscles of the eye and sphincter anus. This, however, gradually disappears.

The entire process of an increase of peripheral irritability of muscle is identical, according to Lewandowsky, and justly so, with the isolation phenomena as Munk describes it and which has long been recognized as characteristic of the vegetative nervous system. This is never dependent upon the absence of inhibition and never occurs immediately after isolation of the organ has taken place.

2. *Action, Sensation and Reflex.*—Under normal conditions there is no voluntary control of the activities of the vegetative nervous system, nor do visceral reflexes to mechanical or sensory stimuli occur via the brain or spinal cord in the usual fashion.

3. *Peculiarities of Smooth Muscle.*—The physiology of the irritability of smooth muscle shows (Nagel, Zierl) that the latter is uncommonly reactive to mechanical and thermal stimuli and less reactive to electrical stimuli; the latter must be continuous in character in order to have an influence upon the somewhat sluggishly reacting smooth muscle. Single induction shocks or discharges from a condenser are less active. Interrupted or constantly increasing continuous currents produce reactions. Smooth muscle is particularly susceptible on account of its sluggishness to summated stimuli. All skin stimuli seem to cause *tonic reflexes,* reflex activity of a tetanic or tetanoid character which, as is seen in the goose flesh due to the activity of the pilo erector, does not persist for a long time after the cutaneous stimulation has ceased. The rigor mortis of smooth muscles may last twenty-four hours after death, as is seen by the marked anemia and goose flesh of cadavers.

4. *The Pre- and Postganglionic Branches of the Sympathetic Ganglia.*—It is noteworthy, from a physiological point of view that, as Langley has established, there is but one ganglion between the cerebrospinal axis and the peripheral or internal end organs. Thus any given stimulus must pass through an intermediary station in order to reach the end organ. When the end organ is of a secretory nature, or is motor with smooth muscle, the motor nerve, whether it be sympathetic or autonomic, can only exert its influence on the organ through a vegetative ganglion and through post-ganglionic fibers (Fig. 1).

The results of transection are the same whether the pre-ganglionic or post-ganglionic fiber is cut. The resulting irritability of the periphery occurs more rapidly and more intensely after transection of the post-cellular fiber than after cutting of the pre-cellular. It is noteworthy also that in cutting a branch of the vegetative, or in extirpating a ganglion, that regeneration only

occurs between pre-cellular and pre-cellular, and between post-cellular and post-cellular fibers. Unless this type of regeneration occurs there is no complete disappearance of the manifestations of transection. Some physiologists deny that there is inherent tone in the vegetative ganglia.

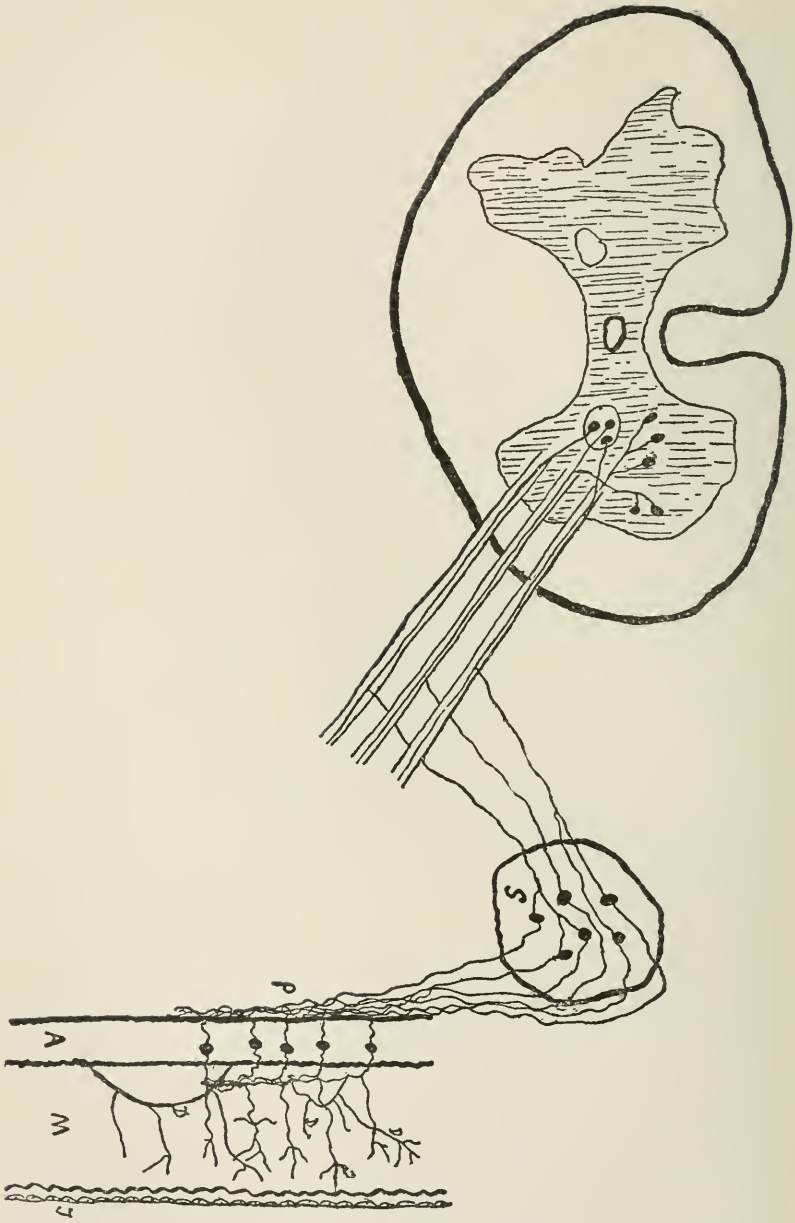
5. *Synapses and Pseudo-Synapses in the Ganglia of the Sympathetic Cord.*—The unity of anatomical structure of the vegetative nervous system implies a unity of pharmacological action which would prove the division between vegetative and sensory motor nerves (Langley & Dickinson). The effects which are brought about by stimulation of the vegetative nerve fibers after they have left the gray matter of the central nervous system, may be stopped at once if a 1 per cent. solution of nicotine is painted upon the ganglion between the place of stimulation and the periphery. Sensori-motor nerve functions are uninfluenced by this procedure. Nicotine, which in large doses paralyzes the ends of all somatic nerves, in small doses acts upon the pre-ganglionic neuron and not upon the post-ganglionic.

If the sympathetic fibers pass through more than one station, *e. g.*, the pupilo-dilator fibers which cross the stellate, inferior and superior cervical ganglia, then painting these ganglia successively with nicotine and stimulating peripherally with a faradic current will show in which ganglia the synapse is placed; that is to say, where the sympathetic fiber does not pass through but is broken and comes in contact with a new physiological neuron.

In the above cited example, painting with nicotine only destroys the electrical conductivity of the pupillary fibers when nicotine is painted upon the superior cervical ganglion. The results of pharmacological methods are quite in accord with the degeneration anatomical method.

We are indebted for our knowledge of most of the anatomical bases of the reflex tracts, which we shall consider, to the animal experiments of Langley and his coworkers. They worked out the central origin and the peripheral extension of the vertebral sympathetic ganglia by means of the nicotine method.

6. *The Myoneural Junctional Tissues.*—Pharmacological experiments with the paralyzing action of nicotine and the stimulating action of adrenalin (which stimulates all ends of the sympathetic system) have shown a further physiological characteristic (Wesseley, Langley, Lewandowsky). Manifestations of the above named substances could be obtained months or even a year after extirpation of the ganglia, or after degeneration following transection of either



Course of the Vegetative Nerve Fibers. (Rudzki & Hornowski.)

pre-cellular or post-cellular fibers. Adrenalin does not act on every nervous part of the doubly innervated end organ; that is, upon the sympathetic and autonomic. It only acts upon the end organs which are innervated by the sympathetic; consequently, the toxic action does not occur upon the degenerated nerve ending but upon a chemically differentiated part of the end organ which is in some ways associated with the sympathetic nerve endings. This has been called by Dickinson, Langley and Elliott *neuro-muscular end-plate*.

This substance which is placed between nerve endings and the smooth muscle cells, has also been called *myo-neural junction* by Froelich.

7. *Distinctive Characteristics of Vegetative Reflexes.*—Organic motor reflexes travel via the vegetative nerve and are accomplished with the aid of involuntary muscle (scrotal reflex, colonic reflex, internal anal reflex, etc.). The reflex contraction of a smooth muscle is slow in comparison to the energetic reflex activity of a cross-striated voluntary muscle. In many reflexes, as for example the cilio-spinal, the reflex activity is only carried out by smooth muscle; in others, *e. g.*, the bladder reflex, the smooth muscle is aided by cross-striated voluntary muscle. In almost all these reflexes the activity may take place more or less completely without any intervention of the central nervous system.

8. *Simple and Visceral Reflex Arcs.*—Some reflex areas are very simple, as for example the esophagus reflex; others are exceedingly complicated, as the erection reflex. Let us take as an example the well-known ejaculation reflex. The stimulation aroused in the sensory end-organ, the glans penis, travels via the N. dorsalis penis and the N. pudendus communis to a spinal ganglion of the lower sacral roots and from here via fibers of the cauda equina to the lumbar ejaculation center where the centripetal part of the arc ends. From this point, the motor activity passes by the lumbar communicating branches and the hypogastric nerves to the pelvic tracts and from here, via gray post-cellular fibers to the powerful smooth musculature of the end organs, the spermatic cord, seminal vesicles and prostate.

The path of the reflex arcs of the head ganglia are very much more complicated because the development of the head from its constituent metameres is not clear cut and the topographical relations of the sympathetic ganglia are extremely complicated. As a paradigm, the reflex which initiates the secretion of the parotid gland via the otic ganglion may be cited. The reflex may be divided as follows: (*a*) The impulse passes through the sensory fibers in the

N. lingualis or the N. mandibularis via the trigeminus to the medulla.[1] (*b*) It also travels through the sensory fibers of the chorda tympani whose trophic center lies in the geniculate ganglia and onward via the N. intermedius to the medulla. (*c*) Finally it travels via the taste fibers which pass via the N. glossopharyngeus to its nucleus in the brain. (Plate III.)

The centrifugal part of the arc is no less complicated than the centripetal. The fibers pass from the nucleus salivatorius inferior in the middle part of the glosso-pharyngeal nerve via the N. tympanicus, the N. petrosus superficialis minor to the otic ganglion and from here via the sheathless post-cellular fibers, which travel with the sensory auriculo-temporal nerve to the parotid ganglia.

The question is: Are such complicated tracts always necessary to the existence of reflex activity in vegetative organs; or do certain reflexes pass from the spinal cord and medulla only to the nerve tissues which are placed near or in the organs themselves.

Müller & Dahl have recently answered this important question in the following fashion: Reflexes which travel solely from the walls of organs via their plexi occur only in those instances in which the sensory stimuli which cause muscular contraction or glandular activity do not reach the brain and scarcely enter consciousness (stomach, intestines, heart, etc.). The reflex arc for these so-called axon reflexes does not lie in the spinal cord but in a vegetative ganglion just without or just within the organ itself. On the other hand the reflex arc is quite complicated in all organs communicating with the outer world, whose activities depend upon exogenous irritation of sensory nerves which carry conscious and localizable sensation. In these instances it is a question of a primary irritation of a sensory nerve which is carried to consciousness and the transference of the stimulus to the vegetative ganglion cells of the cerebrospinal gray axis. The centers for erection, ejaculation, secretion of sweat, secretion of sebum, secretion of saliva, secretion of tears and pupillary contractions are examples. From this point the irritation passes via the corresponding rami communicanti to the peripheral ganglion cell groups which belong to the organ involved. The post-ganglionic tracts are of varying length, from one millimeter to several centimeters and even longer according to the locality of the ganglion cell which has interrupted the path. Thus the synapse may lie very close to the end organ, or it may be very far from it.

9. *Summated Reflexes.*—Some vegetative reflexes are produced by a single stimulus; *e. g.,* the secretion of saliva. Others, however,

[1] The path is then to the pons and thence to the nucleus salivatorius inferior.

such as the ejaculation of spermatozoa, require summated stimuli. In summated stimulation, the impulse begins at the end of the summation and travels from the vegetative centers to the neighboring spinal, or bulbar centers, or cross-striated musculature. For example, the act of vomiting, an anti-peristaltic contraction of the smooth musculature of the stomach, is followed by contractions of the voluntary pharyngeal muscle. Another example of the contraction of the cross-striated voluntary muscle of the constrictor urethræ, the bulbo- and ischiocavernosus, the muscles of the legs and back, subsequent to the contraction of the smooth muscle of the seminal vesicles, was deferens and prostrate.

These parallel manifestations which follow summated stimuli do not alter in the least the principal mechanism of the vegetative reflexes.

10. *Character of Sheathed and Unsheathed Fibers.*—There are many exceptions to the general rule that the preganglionic tracts are sheathed, the post-ganglionic, sheathless. Thus far examined, some of the pre-cellular esophageal and cardiac branches are gray and, on the other hand, some of the post-cellular ciliary and mesenteric nerves are white. The sheathed fibers of the ramus communicans albus are to be considered as those fibers which are pre-ganglionic and through which the spinal cord exerts its influence upon the vegetative ganglia and thus upon the nerves which spread to the corresponding end organ. The white branches are thus motor, centrifugal. The gray fibers, the rami communicantes grisei which travel peripheralward, are also motor in character. They regulate the activity of the vegetative structures of the skin and of the visceral organs of the cranial, thoracic and abdominal cavities through the intermediary station of the ganglia in the sympathetic cord.

11. *Connections Between the Sensory and Vegetative Systems.*—There are normally sheathless fibers springing from the gray branches or from the ganglia of the sympathetic cord whose path is spinalward or to the sensory spinal ganglia. We may only guess their function at the present time. These anastomoses may either carry recurrent nerves to the blood vessels of the vertebral canal, or sensory centripetal sympathetic fibers.

The communication which exists between both systems, that is between the sensory tracts and the vegetative ganglia, may be observed in all the cranial ganglia. An example of this is the ciliary ganglion whose small branch (radix longus) passes to a branch of the first branch of the trigeminal nerve (n. nasociliaris).

The microscopic course of these fibers in the ganglia is not clear up to now since many authors have been of the opinion that there were no sensory centripetal elements among the fibers coming from the ganglion cells and that the sensory fibers going to the ganglia did not end therein but passed through or were merely mechanically associated. Experimental investigation with extirpation of vegetative ganglia (ganglion stellatum, ganglion cervicale, ganglion ciliare) and subsequent careful examination of the cerebrospinal axis, or experiments which disturb the sensory supply of an organ with subsequent examination of the corresponding vegetative ganglia, have not as yet yielded harmonious results.

Whether the sympathetic is really exclusively motor in character, centrifugal, whether the sensory impulses from vegetative organs pass through the customary posterior routes, and the sensory nerves to the cerebrospinal axis will be discussed later.

12. *Relation of Bloodvessels to the Sympathetic.*—The "anlage" of the sympathetic nervous system stands, as is well known, in close relationship with the vascular system in all parts of the body. The maintaining of the close proximity of the sympathetic cord to the neighboring blood vessels is still obscure, in spite of the fact that post-cellular, sheathless nerve bundles or plexi, regularly pass to these.

An example of this may be found in all the intracranial ganglia, *e. g.,* the cilary ganglion sends a fine branch (radix sympathica) to the ophthalmic plexus which winds around one of the cranial blood vessels, the ophthalmic artery. Whether stimuli are carried by these fibers from the plexus to the ganglion, or whether stimuli pass from the ganglion to the distribution of the vessels is still, physiologically speaking, unknown.

13. *The Function of the Ganglia in the Vegetative System.*—This is not entirely understood. Outside of what has been mentioned above concerning the ganglia of the sympathetic cord, it may be said that they regulate the activity of the peripheral vessels, the sweat glands, the skin muscles, and also send fibers to all the internal organs and the large vessels of the thoracic, abdominal and pelvic cavities. All the blood vessels of the cranial cavity are supplied with nerves which have their origin in mesencephalic and bulbar parts of the vegetative nervous system.

Outside of these, the following structures exist: (*a*) Ciliary ganglion lying in the posterior part of the orbit which supplies the sphincter iridis and the ciliary muscle; (*b*) the spheno-palatine ganglia lying on the pterygo-palatine fossa which supplies the lachrymal gland and the mucous glands of the naso-pharynx; (*c*) the

otic ganglia lying under the foramen ovale which supplies the parotid gland; (*d*) the submaxillary and sublingual ganglia which supply the corresponding glands; (*e*) the autonomic ganglia (the bulbar part of the vagus domain) which lie in organs and which supply the glands and muscles of the trachea, the bronchi, the heart muscle and the gastrointestinal tract from the mouth to the descending colon (Fig. 1); (*f*) the ganglion mesentericum inferium, hypogastricum and hemorrhoidale which lie in the upper and lower parts of the pelvis, supplying the muscles and glands of the descending colon, the sigmoid, the anus, the genital apparatus and the blood vessels thereunto belonging.

14. *Functions of Individual Ganglion Cells.*—It is not possible to identify the individual functions of the cells of a ganglion, when that ganglion has cells whose paths go to different organs and control different functions.

Even the significance of the vegetative paths is not entirely clear. L. Müller observes quite justly that we do not know whether these tracts merely serve the purpose of transferring impulses coming from the spinal cord or whether they are also reflex paths bearing sensory impulses from internal organs which give rise to motor impulses. This much is certain, that after exclusion of the abdominal and cord ganglia of the sympathetic system, such organs as the heart, blood vessels, stomach and intestines continue their activity sufficiently to maintain life.

Inhibitory and accelerator activities are to be ascribed to the vagus and sympathetic nerves, while the initiation of activity seems to lie in the ganglion cells of the organs themselves.

15. *Stimuli of the Vegetative.*—In addition to the above-mentioned sensory stimuli, conscious or unconscious, and exogenous pharmacological stimuli as pilocarpin, atropin and nicotin, there are endogenous stimuli which affect the activity of the vegetative nervous system. These are internal secretions as thyreoiodo globulin, adrenalin and the peristaltic hormone.[2]

16. *Cerebral Stimuli.*—The intense reaction which all vegetative end-organs show subsequent to stimuli of cerebral origin, as for example, pain or rapid changes in the emotional sphere, is certainly a physiological characteristic. The reaction manifests itself clinically in terror, fear, pain, anxiety, anticipation, shame, annoyance and joy. The activities of the heart, pupil, vasomotors, sweat glands, gastro-intestinal tract, bladder, tear glands and sebaceous glands, etc., are considerably altered.

[2] Cholin may be added to these.

H. Nusbaum states, and quite justly, that we can have no psychic experience of any kind, joy, sorrow or any other without there being reactions of a definite nature in our body. Strange as it may seem, it is true nevertheless that we should be without shame did we not blush, and without rage if our muscles did not contract, our heart beat more rapidly and thump in our breasts, and if we had not all those other changes in our vegetative organs which accompany the emotional activity of rage. "That the mind acts upon the body and the body acts upon the mind in that important sphere of psychic activity, the emotional, is quite clear."

It is significant that this psychoreflex manifests itself in many ways. The different emotional states have qualitatively different manifestations in various parts of the body.

That which applies to sensory stimuli and emotions also applies to every mental act of the individual. Every psychic activity, every voluntary impulse, every fixation of attention, every stimulating idea brings with it a reaction, for all psychic activites are accompanied by emotional variations and feelings. We are not only governed by pure sensory stimulation, but also by higher intellectual, ethical and esthetic feelings.

The proof of this which lies in the older studies upon psychophysical parallelism promises to be further confirmed in the future thanks to the more recent studies concerning the pupil (continuous pupillary activity) and the vasomotors (variations in the blood volume in the brain and at the periphery). The continual minute oscillations of the vegetative nervous system bear witness that the sum of stimuli going to the central nervous system is always varying; that the tone of the vegetative tracts is always varying (L. Müller), that the mirror of our consciousness, *i. e.,* our vegetative balance is never quite stationary (Bumke).

17. *Antagonism of Autonomic and Sympathetic.*—There exists a further physiological fact of the greatest importance in regard to the vegetative nervous system, that is, a definite antagonism between its various parts. This antagonism has been recognized for some time. The newer researches upon its significance promise to be of great clinical value.

Anatomical investigations by the histological method and pharmacological investigations by the nicotine method have separated the vegetative and sensori-motor systems. Further studies have shown that the vegetative nervous system itself may be divided both anatomically and physiologically into two elements, the sympathetic and the autonomic.

Let us see how the physiologists, who of late years have devoted much attention to this subject, have established this division and how they define it anatomically, physiologically and pharmacologically. The definition is quite empirical and therefore somewhat incomplete.

"Autonomic fibers are all efferent fibers of the vegetative system which are not sympathetic" is the statement of Froelich, who draws his conclusions from his own researches and from results of the pharmacologists, Meyer and Gottlieb. "Those organs which are innervated by the sympathetic include all involuntary organs whose innervation is derived from the thoracico-lumbar spinal cord [DI to LIV]. All other nerve tracts which supply smooth muscle, glands and heart muscle are autonomic." This is another of Froelich's definitions. He goes on: "The autonomic system proceeds from various parts of the cerebrospinal axis. The uppermost part springs from the midbrain, goes to the ciliary ganglion and to the smooth muscle of the eye. This is designated the midbrain autonomic. The second part receives fibers which travel by the facial nerve and pass into the chorda tympani to the mucous membrane of the mouth and to the salivary glands. The chorda tympani is a part of the bulbar autonomic system. The glossopharyngeal and vagus nerves also belong to this part of the autonomic. The latter nerve supplies the thoracic viscera and the viscera in the upper part of the abdominal cavity. The pelvic nerve arises from the sacral part of the spinal cord, particularly from its first two segments. This nerve constitutes the sacral autonomic system. It supplies the viscera of the pelvis and the genital organs.

Between the parts of the spinal cord which have been described there are areas having nothing to do with the vegetative nervous system. One may surmise from this that the cranial autonomic had its origin far cephalad and then wandered caudad. It innervates the entire gastro-intestinal tract as far as the descending colon as well as all organs which had their origin in the digestive tube, as for example the lungs. The sacral part of the autonomic arose from the caudal end of the cerebrospinal axis and developed upward from the anal region until it met the cranial part in the colon region. Between lies the sympathetic, which with few exceptions reaches and supplies all involuntary organs of the body and with varying degree."

Eppinger and Hess, the Vienna clinicians of the school of v. Noorden, basing their observations upon the older work of the English physiologists state: "The vegetative nervous system may be defined both anatomically and functionally. Those fibers which

arise in the thoracic and upper lumbar segments of the spinal cord and the sympathetic cord comprise an anatomical unit. After the fibers have left the sympathetic cord anatomical differentiation is difficult, for the sympathetic fibers are mixed with others on their way to the end organs. The second anatomical entity is characterized by the fact that its fibers arise from the midbrain and medulla as well as from the sacral cord and that they have no relation to the sympathetic cord."

On gross anatomical grounds the origin is divided into three parts, midbrain, bulbar and sacral. The midbrain part passes into the oculomotor nerve, is interrupted in the ciliary ganglion and supplies certain parts of the eye. The bulbar part passes into the facial and glossopharyngeal nerves and supplies fibers to the salivary glands and the vasodilator muscles of the head. The most important nerve of the bulbar part is the vagus, the main nerve of the viscera. It supplies fibers to the heart, bronchial tubes, esophagus, stomach, intestine and pancreas. The sacral part, spoken of anatomically as the pelvic nerve, supplies fibers to the descending colon, the sigmoid, anus, bladder and genital organs.

For the sake of brevity it is customary to speak of all fibers which pass through the sympathetic cord as the sympathetic while all other fibers comprise the autonomic or "extended vagus." It is noteworthy in this connection that it is comparatively easy to separate the two systems at the cerebrospinal axis, while it is exceedingly difficult, almost impossible, to separate them at the periphery.[3]

18. *Classes of Fibers in the Vegetative.*—There are two general classes of fibers in both the autonomic and the sympathetic systems, (*a*) positive, stimulating, vaso-viscero-glandulomotor fibers, (*b*) negative, inhibitory, vaso-viscero-glanduloinhibitory fibers. The normal state of irritability of the ganglion cells is regulated through delicate activities of inhibition and stimulation, so that the apparently superfluous inhibitory influences are in reality an invaluable psychic property of the central nervous system.

19. *Double Formation of End Organs.*—Another noteworthy characteristic of vegetative end organs is that they are supplied not only by all the paths going through the sympathetic cord (sympathetic fibers) but also by the fibers of the second system (autonomic). Thus practically no involuntarily acting organ exists which is not doubly innervated.[4]

[3] See Eppinger and Hess. Vagotonia. Tr. by Krauss and Jelliffe. Nervous and Mental Disease Monograph Series No. 21.

[4] For an interesting and enlightening discussion of this matter see Gaskell, The Involuntary Nervous System, 1916.

The sweat glands, pilomotor muscles and vascular muscles of the viscera form an exception in that they are only supplied by the sympathetic.[4]

However, pharmacological proof, which many consider most important, indicates that these structures, particularly the sweat glands, are innervated by the autonomic. It is in our opinion quite improbable on a priori grounds that there should be any exception to the rule that all organs are doubly innervated. We are rather inclined to believe that diffusely located ganglion cells exist in the cerebrospinal axis, which belong neither to the mesencephalic, bulbar nor sacral groups of autonomic structures and which supply the sweat glands, pilomotor muscles and vascular muscles with autonomic fibers. The apparently strange division of the autonomic would be found untrue by this rational theory.

20. *Effects of Electrical Stimulation Upon the Vegetative.*— Simple investigations with electrical stimulation showed that in many organs stimulation of one system served to inhibit the activities of the other. Thus both systems, the sympathetic and the autonomic, showed physiological antagonism. Impulses going to organs from the sympathetic as a rule acted contrariwise to stimuli from the autonomic. As an example: The bulbar autonomics have a vasodilator effect upon the blood vessels of the head, while the cervical sympathetic acts in a vasoconstrictor fashion. Some doubly innervated organs do not have muscles which act exactly oppositely to one another, *i. e.,* like the sphincter and dilator pupillæ, but there is but one group of muscles. Yet stimulation of one part of the vegetative will cause shortening, of the other part lengthening of the muscle.

The double innervation is a very important characteristic, one which is not found in the psychomotor system. The cervico-thoracico-sympathetic fibers are opposed functionally and pharmacologically to the cranial autonomic fibers, and the thoracico-lumbar fibers have the same relation to the sacral autonomic, the pelvic nerve.

(*a*) The pupil, tear glands, salivary glands, and cerebral blood vessels are supplied by both the cranial autonomic and the cervical sympathetic.

(*b*) The heart, stomach and intestines are supplied by the autonomic vagus nerve and the thoracic sympathetic.

(*c*) The recto-vesico-genital apparatus is supplied by the sacral autonomic system and the lumbar sympathetic. In a word the autonomic and sympathetic are like an object and its mirrored image, are like the positive and negative of a photograph (Froelich).

Just as there are physiologically opposed stimuli, so there are chemically opposed stimuli both of exogenous and endogenous origin (atropin and pilocarpin, adrenalin and cholin). If two oppositely acting substances are used at once the more powerful gains the upper hand just as in experimental stimulation of the autonomic and sympathetic nerves to the heart, the influence of the more powerful vagus predominates, causing brachycardia, and in the eye the autonomic fibers in the oculomotor nerve predominate causing miosis.

The normal progress of activity in visceral organs is therefore an orderly result of oppositely acting stimulation. The purpose of this antagonism is to prevent the activity of the various organs from going to one extreme or the other.

21. *Anatomy of the Autonomic.*—Since the nerves of both systems are mixed with other nerves on their way to organs, the relations of the nerves to each organ must be worked out anatomically, physiologically and pharmacologically. The following points which were not gone into in detail in the discussion of the anatomy of the sympathetic are of importance in regard to the autonomic.

(*a*) In the midbrain the autonomic is composed of those fibers in the oculomotor nerve which supply the sphincter pupillæ (miosis), the ciliary muscle [accommodation spasm] and in part the levator palpebræ (widening the lid slits).

(*b*) For the medulla the tracts going by way of the chorda tympani to the salivary glands and by way of the N. lacrimalis to the lacrimal glands are worth noting. The vagus, which supplies the lungs, heart and gastro-intestinal tract is also of great importance. This nerve contracts the smooth muscle of the bronchi. It furnishes inhibitory fibers to the heart, which act in every way antagonistically to the sympathetic accelerators. The four functions of the heart, chronotropic, inotropic, bathmotropic and dromotropic, are all affected. The vagus also contracts the musculature of the upper part of the gastro-intestinal tract, the esophagus, the cardiac sphincter and the sphincter antri pylori. It also increases the peristalsis and secretions of the stomach. In the small intestine the vagus causes emptying movements, more rarely tonic contraction. Its effect upon the smooth muscle of the gall bladder and the excretory duct of the pancreas is to produce intermittent contractions. Stimulation of the vagus branches to the pancreas causes an increase of its secretion.

(*c*) For the spinal cord there are in addition to sympathetic fibers diffusely located autonomic centers for control of the blood vessels of the skin and mucous membranes, the pilomotor muscles and the sweat glands.

(*d*) The centers of the autonomic pelvic nerve lie in the lowest part of the spinal cord. This nerve might be called a lumbosacral vagus. It supplies the descending colon, the sigmoid, the bladder and genitalia. Stimulation causes erection, spasm of the sphincter of the rectum, contraction of the detrusor of the bladder and simultaneous relaxation of the sphincter.

It is most probable that through their influence upon glands of internal secretion (pancreas, thyroid) the autonomic has a considerable influence upon metabolism.

22. *Various Higher Vegetative Centers.*—The midbrain as far as the corpora quadrigemina constitutes the general end station of the vegetative nervous system in the cranial region. Experimentally obtained facts gathered in recent years making it probable that the hypothalamus, *i. e.,* the region lying between the epiphysis and the hypophysis, contains synapses for the vegetative pathways.

Destruction of the corpora mamillaria causes polyuria (Eckhardt), of the thalamus, hyperthermia (Jung), of the lateral area of the gray matter on the floor of the midbrain, dilatation of the pupil and widening of the lid slit (Karplus-Kreidl). Stimulation of the ventricular floor in the region of the hypophysis brings about contraction of the bladder, the intestines and uterus (Frankl-Hochwart and Froelich), while stimulation of the tuber cinereum produces dyspnea and arrest of the heart's action, followed by bradycardia (Aschner). Lesions of the floor of the midbrain induce marked metabolic and trophic changes in young and adult animals (genital dysplasia of the ovaries and testes, retardation of growth) and puncture of the floor of the third ventricle causes intense glycosuria similar to the Claude Bernard puncture of the floor of the fourth ventricle (Aschner). Simultaneous section of the distal ends of the sympathetic (NN splanchnici) prevents the occurrence of this glycosuria of hypothalamic origin as well as any glycosuria which may be caused by stimulation proximal to the place of section. As will be emphasized later, this glycosuria is an adrenalin glycosuria and is accompanied by a marked reduction of the chromaffin substance of the adrenals.

This experimental evidence, as well as the clinical observations and the after effects of operations on tumors and hydrocephalus of the midbrain region, lead to the following conclusions. Vegetative nerve tracts controlling visceral activities extend into the brain as far up as the third ventricle. Trophic and metabolic disturbances which have hitherto been ascribed to dyspituitarism may also have their origin in a disturbance of the neighboring part of the brain,

the hypothalamus. This possibly acts as a regulating center for glands of internal secretion and for the vasomotors of the brain.

23. *The Sensory Innervation of the Vegetative Systems.*—This differs considerably from cutaneous sensation and follows different laws. Since its semiology has a wide bearing upon many problems, it will be discussed at some length.

It has become customary to speak of the vegetative system as purely motor, for the reason that the sensory fibers from the viscera pass into the cerebrospinal axis *via* a posterior root ganglion or what corresponds to it, the Gasserian ganglion.

What are the general relations of the sensory elements of the vegetative system and their relations to motor and secretory activity in particular? Most people, particularly if normal, never experience any sensation from the internal viscera. Others, particularly the neuropathic, learn by practice to recognize such sensations. Motor and secretory activity is never voluntary and is usually reflex, in response to some sensory stimulus. These stimuli, when they are carried to consciousness by the somatic nervous system, travel by the usual route. Examples are the sensation of light which contracts the pupil, stimulation of the conjunctiva with a flow of tears, stimulation of the glans penis with ejaculation, local application of heat with sweating, local application of cold with blanching, taste stimulation with salivation, stimulation of the mucous membrane of the bronchial tree with bronchospasm. If the primary stimulus causing the reflex comes from the vegetative nervous system, it remains unconscious. Examples are activity of the pharyngeal glands, stomach, intestine, gall-bladder and ureter.

When the sensory stimuli pass to consciousness they are converted into reflex stimuli in the gray matter of the spinal cord. When sensory stimuli *do not* pass to consciousness, the reflex is accomplished most probably in the organ or the neighborhood of the organ itself. The facts that normal peristalsis, secretion and digestion go on when all nerves to the intestine and stomach are cut, and the continuation of cardiac activity after the autonomic and sympathetic supply is cut are evidences in favor of this hypothesis. When an organ acts periodically, the impulses of nervous origin recur quite regularly. L. Müller strengthens this idea as far as the intracardiac nervous system by saying that "there are many ganglion cells at the place at which the cardiac impulse is initiated, the sinus node, and at the place at which the impulse passes from the auricle to the ventricle, the node of Tawara."

The question whether the organs of the vegetative nervous sys-

tem can produce sensory stimuli, stimuli which may become conscious and particularly stimuli of pain, has been discussed in the fields of both physiology and pathology for many years. As early as the seventeenth, eighteenth and nineteenth centuries, Harvey, Albert von Haller and Weber maintained on the basis of their experiments that internal organs, particularly the heart and intestines, were unreactive as far as sensation was concerned.

In the last decade, Lennander, Wilms and others, in several contributions concluded on the evidence obtained in laparotomies done under local anesthesia that the internal organs of the abdominal cavity have no sensory supply. It was thought that the results obtained by stimulating mechanically or chemically, that is, absence of pain, could be compared to the stimuli occurring under normal conditions. Lennander denied that there exists any sensation in either the intestine or the visceral peritoneum. He showed that the parietal peritoneum was supplied with pain fibers. The painlessness of many operative procedures upon the organs of the thoracic and abdominal cavities led Lennander's followers to conclude that no internal organs were sensitive to pain, while all parts in these cavities which are supplied by the spinal nerves, as the parietal peritoneum and pleura, were sensitive to pain.

Many facts pointed against Lennander's contention, such as sensitiveness to pain on pressure upon an inflamed organ, severe tabetic gastric crises, enteralgias of other nervous diseases. The simplest explanation of these contradictory facts is offered by Lewandowsky. He maintained that the normal daily stimuli from the always active organs reached the spinal cord *via* the posterior ganglia. Such stimuli include the centripetal impulses of osmosis, diffusion, capillarity, filtration, movement of blood and lymph, variations in surface tension, chemical molecular intraorganic processes, etc. These stimuli only pass cerebralward when the degree of stimulation passes a certain level. Then they become painful stimuli as colic, cardiac pain, the pain resulting from transient anemia and hyperemia of organs and the nerves supplying them. Analogously, we do not feel the continual rubbing of our clothes on our body, the temperature about us, if it be not of extreme grade, taste in our mouths if it be not extreme, the contractions of our muscles if they be not cramplike.

From our present knowledge, we must conclude that the skin and the visible and external mucous membranes are more sensitive and are better equipped to react to external noxæ and variations of all kinds than the internal organs of the body.

One thing must not be forgotten in drawing conclusions from

animal experimentation, namely that extra-physiological inadequate or extreme stimuli are used to test cardiac or intestinal sensation as incisions, electric currents, great heat or strong acids. Internal organs have sensations peculiar to themselves, a specific sensibility. This, like external structures whose nerve supply differs with their peculiar needs, is adequate to the needs of the organs, but different from that of external organs and can by no means be measured by the same standards. For example, Zimmermann found that the esophagus, stomach, ureters and bladder were sensitive to changes in pressure, a warning mechanism, no doubt. Yet, heat, cold and irritation aroused no reaction, no sensory fibers existed for these stimuli.

Some investigators as Mackenzie and Head assume the existence of centripetal fibers from organs to spinal cord. On this basis, a middle position between no sensation at all and a specific sensation is taken. This school believes that the fibers from organs to spinal cord do not pass directly to the cortex, but that they first go to the spinal cord and from there the sensation may be relayed to the cortex. This theory has become extremely popular. It accounts for reflex pains occurring in visceral disease, pains which are often not felt in the organs themselves, or not only in them, but are also very definitely localized in some skin area. This area corresponds to the spinal cord segment which receives the nerve fibers from the organ involved. There is no doubt of the existence of these hyperalgesic areas of Head, the only doubtful element being the explanation of the entire mechanism of their occurrence. They were described by others before Head, Bassereau (1847), Beau (1866) and Lange. The English authors believed the occurrence of these hyperalgesic areas to be due to the passage of abnormally strong stimuli from the organs to the spinal cord, thus making the sensory fibers there much more sensitive. From this, the corresponding skin areas became over-sensitive or hyperalgesic.

The conclusion from these last mentioned facts is as follows: There are fibers passing from internal organs *via* the posterior ganglia to the spinal cord which do not give any definite sensation but are sensory in nature and are not to be confused with any vegetative fibers passing to the organs. These fibers are activated by abnormally strong stimuli. It is noteworthy that the Head zones are never as sensitive when the pain stimulus comes merely from the spinal cord fibers, as when they come from some stimulation of the cerebrospinal axis impulses from vegetative organs.

Newmann attempted to discover the localization of painful sen-

sations by experimental methods. He used various means, pinching, striking with fine hot rods, faradization, painting with acetic acid. He applied these various stimuli to all parts of the mesentery, suspensory ligaments and parietal coverings of the internal organs of the frog. Some experiments were tried on dogs. He found all organs but the spleen and kidneys sensitive, giving a reaction a definite time after the abdomen was opened. The reaction consisted in powerful reflex movements of the hind legs and the posterior girdle muscles. Newmann states that the sensory fibers for the thoracic cavity pass in the vagus nerve while those for the abdomen pass in the splanchnic nerves. This is shown by the cessation of reflex movements when these nerves are cut. The intestine, moreover, has a mechanism by which stimuli are passed cerebralward *along* the intestine even though its mesentery with its centripetal nerves are separated from it. This Newmann speaks of as transference of stimuli *along* the intestines, *i. e.,* to *other* segments and *then* centralward.

The intestinal wall is composed, going from outward in, of the following layers, longitudinal muscle, Auerbach's plexus, circular muscle and Meissner's plexus. Newmann states that sensation is lost when Auerbach's plexus is destroyed and that intestinal sensation, *i. e.,* the sensory endings of the vegetative reside in it. Whether this sensory function in man is part of the autonomic or sympathetic systems has not as yet been discovered.

L. Müller came to the following conclusions from his work upon the vagus: (1) The contention of Lennander and Wilms that the intestine can give no sensory stimuli without the intervention of the nerve fibers going to the cerebrospinal system from the parietal peritoneum must be definitely abandoned. (2) There is no definite basis for assuming the existence of sensory fibers in the vagus. Since stimulation of the splanchnic nerves causes pain sensations and reflex movements of considerable intensity, these nerves must be considered as sensory in part. The sensory fibers have, as Langley believes, their trophic center in the posterior root ganglia and pass *via* these to the spinal cord.

Normal tactile and chemical stimuli are limited in their effect upon the intestinal wall in that they only provoke motor and secretory reactions. Only under abnormal conditions do sensory stimuli pass to the cerebrospinal axis. If the abdominal wall be stretched (meteorism), the activity of the intestines be obstructed, colicky movements occur like leg cramps, if the blood supply of the intestines be obstructed (embolism of the mesenteric artery)

causing a condition similar to the vasomotor spasm of angina pectoris or the intermittent claudication occurring in the extremities, then severe pain sensations begin. The pains produced are more severe than those produced by simple stimulation of spinal nerves. These sensations are frequently accompanied by signs of abnormal activity in other parts of the vegetative nervous system, as for example, salivation, sweating, pallor of the face, raising of blood pressure.

Severe intestinal pain of purely nervous nature sometimes comes spontaneously (splanchnic neuralgia), the basis being either an intoxication, as lead, or syphilis (tabetic intestinal crises). Rare exceptions are severe intestinal pains without increased peristalsis (lead) and much increased peristalsis without pain (animals all of whose abdominal nervous system has been removed except the sympathetic). Not only under normal but also under abnormal conditions mild stretching feelings are felt in the intestinal tract, especially in the rectum. These lead to active emptying either from above or below.

Sensation in the intestine has according to Müller the same function as sensation in the outer coverings of the body, namely to act as a register of some disturbance and as a protector of the organism against harm. The severe pains lead to rest and sparing of the affected organ. It is interesting to note that intense emotions also have a quieting effect upon the intestine. "The splanchnic," says Müller in concluding, "has the function of transmitting sensations from the intestinal tract to the brain when the former is disturbed and of transmitting sensations from the brain to the ganglia of the intestines when the normal activity of the former is lessened due to fear or anxiety or pain. The splanchnic nerves are therefor the mediators between the activities of the brain and the intestines and carry signs of danger in one to the other."

Froehlich and Meyer on the basis of very exact experimental work have come recently to conclusions somewhat different than Müller's. They tested the pain-bearing paths from the intestines and bladder of dogs. They used a faradic double electrode, a rubber balloon and a 5 per cent. solution of barium chlorid which would cause marked colicky intestinal contractions. They relied upon loud cries and escape movements as a test of the pain. By various transections of the lower spinal cord and removal of posterior roots they were able to show that sensation in the bladder except in the sphincter region was *not* carried by the sympathetic hypogastric nerve or the spinal nerves (NN. pudendi and N. hemor-

rhoidalis post.) but exclusively by the autonomic pelvic nerve. This last sends pain fibers upward to the brain through the sacral spinal roots.

It has been shown that not only stimulation of the parietal peritoneum is a stimulus adequate to produce pain, a fact shown by Lennander, but that stretching of the visceral peritoneum and colicky contractions of the circular intestinal muscle may do the same even in a normal intestine. According to Lennander, pain stimuli cannot reach the brain *via* the splanchnic nerves. This does not exclude the possibility, say Froehlich and Meyer, that the centripetal neurone may pass in the splanchnic nerves to the spinal cord and by means of short motor reflex paths produce effects in either the splanchnic domain itself or in the abdominal muscle innervated by the spinal nerves, effects which are never brought to consciousness. The bulbar autonomic vagus nerve remains as the bearer of sensory stimuli from the intestines as the sacral autonomic pelvic nerve is the bearer of sensory stimuli from the bladder, in fact, from the entire vesico-recto-genital region.

Eppinger and Hess in their study of tabetic crises (gastric, laryngeal, bronchial, vesical, rectal and genital) came to the conclusion that these were almost exclusively due to stimuli in the autonomic system. Severe degenerations are found only in the main branches, the vagus nerve and the pelvic nerve or their branches. The sympathetic system, as for example the ganglionic chain, are free of any such disease. These authors believe, basing their belief upon anatomic-pathological grounds, that it is probable that the tabetic poison which is selective in the involvement of peripheral sensory neurones, also has special affinity for visceral autonomic nerves since they are almost exclusively involved, while the sympathetic is scarcely at all involved.

Forster, for the following reasons, claims sensory fibers in the vagus as well as in the splanchnics. (1) Because hyperesthetic zones (Head zones) are found not only in the thorax and abdomen but also in the anterior and posterior part of the head area in disease of the gastro-intestinal tract. This he believes due to radiation from the medulla (*via* the vagus) into the trigeminal area. (2) Because in patients with complete transverse section of the cord at the cervical level, there is a feeling of pressure and nausea in the stomach upon strong pressure of the fist into the abdomen, in spite of the anesthesia of the skin in this area.

In all probability the vagus carries the specific stomach and intestinal sensations as nausea, while the sympathetic carries ordinary

pain sensations. In tabes then we would expect splanchnic crises more often than vagal crises. The first would show itself by severe pain, hyperesthetic skin zones, increased abdominal and epigastric reflexes, the later by nausea, vomiting and hypersecretion.

Forster argues as follows: If splanchnic crises in tabes are due to stimulation of sensory fibers, the pathological process must lie in the intraradicular part of these fibers through the posterior roots. Operative interference, section of the roots, should have a distinctly beneficial effect. Forster's operation in gastric crises is to cut the sixth, seventh, eighth, and ninth dorsal roots; in intestinal crises, the lower dorsal roots. It is not so simple a matter with vagal crises. Here the sensory fiber change lies somewhere between the sensory ganglion of the vagus (ganglion jugulare) and the entrance of the vagus root into the medulla. A therapeutic effect theoretically could only be obtained by cutting at this place, and, not subdiaphragmatically as recommended by Exner, who bases his contention on the supposition that the crises are not due to sensory hyperirritability but to stimulation of the motor endings in the vagus.

It would be of great value to know the result of every operation of the above nature so as to discover just which of the two nerve tracts (vagus or splanchnic) carries the pain sensations. Heile recommends intradural injections of anesthetic liquids into the foramina vertebralia in order to destroy the function of the posterior roots which seemed to be involved.

If this injection succeeds in allaying the pain of gastric crises, it shows that the pain sensations pass to the spinal cord *via* the rami communicantes. If, however, only anesthesia of the skin occurs, the pain must have been carried centralward *via* the vagus.

What has been said of gastro-intestinal tabetic crises applies equally to other crises if they are of the mixed type and involve both vegetative organs and the motor-sensory segment associated with them. Examples are head, ocular, nasal, pharyngeal, mammary, sebaceous, sweat, vascular, uterine, clitoridal, intestinal, renal and bladder crises.

24. *Types of Vegetative Reflexes.*—The physiological relations between vegetative reflexes and sensations of pain and emotions deserves a closer examination.

In man the viscera not only have a sensory reflex, but also a motor and a visceral reflex (Mackenzie).

I. The *sensory reflex* which serves for protection is composed of a sensory stimulus in the zone of the organ concerned. This is either internal or splanchnic and is pain, though all authors are not agreed upon this, or external or somatic, where pain is readily felt

in the hyperesthetic zones. The following are the characteristics of these sensations of pain.

(*a*) Splanchnic pain usually is in the midline, even if the organ by which it is caused lies on one side or partly so (esophagus, stomach, liver, intestines, kidneys).

(*b*) Contrary to the pain of hyperesthetic zones, splanchnic pain is not relieved by moderate chloroform narcosis.

(*c*) The radiating external pains are never precisely defined.

(*d*) The radiating external pains are felt in deeper structures (muscles, breast) not in the superficial layers of the skin.

(*e*) Artificial stimuli as alcohol, mustard plasters, hot applications, cantharides and the galvanic or faradic currents prevent viscerofugal stimuli from passing through the spinal roots to the hyperalgesic zones. They act as quieting, pain-relieving agents (derivantia et revulsiva).

(*f*) Both types of pain, visceral and radiating, are increased by intense emotions, as fear and anger.

II. The *motor reflex* usually consists in some stimulation in that part of the external musculature corresponding to the organ of stimulation. Examples are contraction of the chest muscles, particularly the large spinal muscles "*signe des spinaux,*" which occurs in pleuritis, and contraction of the abdominal muscles in diseases of the stomach, intestines and liver. Sherrington was one of the first to demonstrate the rôle of the efferent sympathetic nerves in these reflexes. He cut the abdominal visceral nerves and stimulated their central ends. There resulted a distinct contraction of the abdominal musculature corresponding to the nerve which was stimulated. This viscero-motor reflex stimulation gradually disappeared on cutting the posterior roots which carried the stimuli from the visceral nerves.

III. The *organ reflex* is usually a secretory, peristaltic or antiperistaltic stimulation in the organ which is stimulated. Examples are salivation, gastrosuccorrhea, vomiting, accumulation of mucus in the bronchial tree and hiccough. In all these reflexes the primary sensory irritation plays the main rôle (Head, Mackenzie, Forster).

Tabetics often do *not* have these reflexes due to visceral anesthesia. Such failures to respond normally occur in instances like the following: cremaster reflex after stimulation of the testicle, pain and abdominal contractions during parturition, abdominal pain, vomiting and muscle spasm in appendicitis.

The following chart by Mackenzie serves as an aid in the differential diagnosis of visceral disease by means of somatic pain.

Toothache often gives a viscero-sensory hyperesthesia of the cheek.

The pain in the shoulder of the same side as a pneumonia is due to the fact that the sensory innervation of the shoulder comes from the same spinal segments (C 4 C 5) as the phrenic nerve supplying the pleura.

The severe pain of pleuritis caused by deep breathing is not due to pain in the pleura, but to a viscero-motor reflex involving the intercostal and spinal muscles.

In heart disease pain lies in the arm and thoracic region whose sensory supply comes from the same spinal segments (D 3 D 4) as the sympathetic nerves to the heart. The rare occurrence of pain in the skin of the neck and the left neck muscles is due to the afferent vagus fibers which carry the stimuli over into the second and third cervical segments. A more significant viscero-motor heart reflex is the feeling of oppression which results from a radiating spasm of the intercostal muscles. A cardiac organ reflex of less significance is the salivation and profuse urination which occur in angina pectoris, both symptoms due to reflex stimulation of the centers lying near the vagus center in the floor of the fourth ventricle.

The feeling of cold in the stomach after drinking cold water is due to a contraction of the skin blood vessels and is accompanied by a circumscribed area of goose-flesh. Thus there are two visceral reflexes, one pilomotor, the other vasomotor. The viscero-motor reflex contraction of the upper left rectus abdominis in gastric ulcer is explained by the origin of the sympathetic gastric fibers, D 6, D 7. The heartburn which results from regurgitation into the esophagus localizes itself one segment higher. Pain of gastric origin rarely is localized according to the position of the ulcer or carcinoma. It is usually in the median line, and in cardiac, fundal and pyloric disease is found in the upper, middle and lower part of the epigastrium.

A very interesting organ reflex in appendicitis is difficulty of urination which is not infrequently associated with the hyperesthesia over McBurney's point.

Pain in the upper arm in liver disease is explained by the origin in the same spinal cord segment, C 4, of the nerves to the arm and the phrenic nerve to the liver.

In disease of the kidney pelvis and ureters the viscero-sensory reflex passes to the testicles, the viscero-motor to the cremaster and transverse muscles since the nerve supply is derived from the eleventh and twelfth dorsal and first and second lumbar segments.

For this reason the testicles and the scrotum are sensitive in cases of nephrolithiasis.

Since the upper portion of the bladder is developed from the allantois (L 2) and the lower from the cloaca (S 2), the reflex pain depends upon the site of the disease. Sometimes it is above the pubic bone, sometimes in the penis and perineum. The viscero-motor reflex causes spasm of the sphincter ani.

Reflex pain from the uterus and ovaries lies in the lower abdomen.

Pain in the knee in hip-joint disease is due to the identity of the spinal segment supplying fibers to these two joints, L 4. The synovia are supposed to be supplied by the vegetative nervous system just as the peritoneum.

25. *The Effect of Pain.*—A subject which stands closely related to that which has just been discussed, the sensibility of organs, is the effect of intense pain, particularly visceral pain, upon the activities of vegetative nerves. This does not relate at all to the effect upon the other part of the nervous system, the somatic or "animal." It has been shown that a temporary alteration of vegetative nervous system activity always follows severe pain. This alteration occurs not only in the organs innervated by the head ganglia, but also in those innervated by the thoracic and abdominal ganglia. Pain causes tears, buccal secretion, salivation, dilatation of the pupil, reddening of the face, palpitation, anacidity (Pawlow), uterine and gastro-intestinal inactivity (Holz).[5]

This inhibition of visceral activity occurs: (1) *Via* the sympathetic nervous system, not the autonomic. Cutting the splanchnic nerve prevents its occurrence. (2) Irrespective of the source of the pain sensations, skin, mucous membranes, nerves or body cavities. (3) Irrespective of whether the pain may have reached consciousness or not. This last fact has been determined by the fact that organ reactions to pain occur even if the upper spinal cord be severed or the cerebral cortices be extirpated. The inhibitory reflexes must take place in the spinal cord. L. Müller concludes very justly that "since all the sensory nerves cannot be connected by intraspinal fibers to all the vegetative tracts, it must follow that marked sensory stimuli cause a general alteration of the bio-electrical state of the spinal cord, which in turn by means of the rami communicantes causes inhibition *via* the visceral nerves."

The subject of biotonus and the power of the cerebrospinal ner-

[5] Tr. note. For a recent excellent treatise on this subject from the standpoint of "conscious" emotional reactions see W. G. Cannon. "Bodily Changes in Pain, Hunger, Fear and Rage." Appleton & Co., 1915.

vous system to diffuse nerve impulses will receive more attention later in speaking of the localization of cortical vegetative centers and the influences of emotions upon vegetative nerves. Biotonus should not be confused with "vagotonus" and "sympathicotonus" which will be discussed later as well.

26. *The Influence of the Cortex.*—Several very important questions in the physiology of the vegetative nervous system will receive consideration in this last section. They are (I) the location of the sympathetic centers *i. e.,* the psycho-vegetative centers in the cortex analogous to psychomotor centers, (II) the influence of the mind upon the tone of the vegetative nervous system, (III) the influence of emotion upon vegetative nerve activities.

I. Have internal and external visceral organs cortical centers like voluntary muscles and the sensory functions of the skin? In order to answer this question the relations of the vagus will be considered, since its anatomical relations, its viscero-bulbo-thalamo-cortical parts, have been very carefully studied. The vagus is a mixed nerve having three nuclei whose embryological development is different. The motor nucleus ambiguus corresponds to the anterior horn, the sensory nucleus solitarius to the posterior horn and the visceral nucleus dorsalis vagi to the vegetative nerve cell group which lies in the lateral gray matter of the spinal cord. There is no need of entering a discussion as to the reason of the inclusion of sensory fibers in the vagus trunk, nor as to their philogenetic relations. What is important is that the sensory fibers supply the mucous membranes of several cervical and thoracic organs—and that they continue upward through the thalamus to the cerebral cortex. We also know that there is a cortical center for the fibers to the voluntary muscles of the pharynx and larynx, the pharyngo-laryngeal center. This we know exists whether it came at a period when these muscles became striated or whether it existed when they were still involuntary, unstriated muscles. The philogenetic relations do not alter the facts. A cortical representation of the visceral part of the vagus, of the cardiac, bronchial, pulmonary and gastric fibers of the vagus is questionable. The same question of course arises in connection with the other autonomic and sympathetic fibers which have to do with the excretory and secretory organs of the skin and body cavities. There are now two quite opposite views upon this subject. One school is headed by Bechterew, the other by Pawlow and L. Müller.

Bechterew's school tried to arrive at a conclusion by investigating association reflexes. Association reflexes according to this

school consist in a reaction which is not determined by either the strength or the quality of the external stimulus, but by the relation of this stimulus to other reflexes in the past, *i. e.,* a relation that has been often repeated and whose repetition occurs in the same manner as the reactions produced by habit. The hissing of a snake produces in us an associative reflex which manifests itself in an intense motor reaction not because of the loudness or softness of the noise, not on account of the hissing itself, but because the hissing is associated with the possibility of a bite. The presence of a cat causes a dog to run because of past experiences with the cat's claws. The smell and sight of appetizing food stimulates the appetite and starts gastric secretion.

Since vegetative functions are concerned with the most vital of body processes, processes which are activated by simple reflexes, extirpation of the cortex does not interfere with their activity, does not cause any paralysis as extirpation of the motor cortex supplying the extremities. But there does result a great defect of nerve activity in so far as associative reflexes go.

If we remove in the dog what Bechterew regards as the cortex representing respiratory activities and remove both centers, respiration proceeds normally due to the presence of the spinal, the coordinating medullary and the subcortical midbrain centers. The respiratory reflex to artificial as well as normal sensory stimuli is the same as before. But the *psychoreflex,* the associative reflex, is absent. The presence of a cat does not cause the intense motor effect upon respiration which occurred in the normal dog under like circumstances.

If both sexual centers in the upper third of the gyrus postcruciatus be removed in a dog, the normal reaction of the penis to mechanical stimulation remains, but the normal psychoreflex due to the presence of a bitch in heat is absent.

If the pupillary center in the frontal lobes be removed, certain stimuli which normally frighten the animal, as threatening with a stick or whip, do not cause dilatation of the pupil, a reaction which occurs even if the third nerve be cut.

Any attempt to obtain the ordinary reflex salivation in a dog with a salivary fistula whose cortical centers for salivation have been removed is successful. Stimuli of taste and smell always give a profuse reflex salivation. But the psychoreflex is absent. Showing the dog food in a closed glass vessel, placing odorless food before him, rattling plates or other dishes provoke no reflex salivation.

There is also supposed to be a cortical center for gastric secre-

tion whose absence prevents the occurrence of psychogenic gastric juice due to the stimulation of food not yet eaten. The other gastric reactions remain unaltered.

Experimentation with lactating sheep has shown a cortical center for milk production in the frontal lobes. After these centers have been bilaterally removed, the sheep does not nurse its lamb either upon seeing it or hearing it cry. This she would do before the operation.

These experiments were subsequently elaborated and modified. Where at first the salivation appeared only on seeing food and simultaneous sensory stimulation of a quite different nature, later the sensory stimulation sufficed to bring about the reflex stimulation (artificial association reflex). Such sensory stimuli are sticking the leg, cooling the chest, smelling musk, the sound of the note C, etc.

Bechterew concluded from the above and similar experiments upon the cortex cerebri that visceral tracts, motor and secretory, have a central cortical representation. Pawlow reached conclusions based upon what he calls natural and artificial association reflexes, which are diametrically opposed to those of Bechterew. These opposite conclusions were based on the observations that the absence of psychoreflexes was but transitory and shortlived.

L. Müller is also skeptical as to the validity of the above experiments. In his opinion neither physiology, histology nor pathology has given us any definite basis for believing that there are cortical centers for internal organs.

Faradic stimulation of the cerebral cortex causes mydriasis, salivation, intestinal inhibition, etc., for the same reason that stimulation of a sensory nerve will produce these results in the vegetative nervous system. There are neither cortical centers nor sympathetic spinal cord tracts. External skin structures (vasomotor muscle, pilomotor muscle and sweat glands) and the internal viscera receive so many fibers from the rami communicantes of the spinal cord metameres—there are over forty—" that the visceral tracts, if they did pass in the lateral columns of the spinal cord would take up considerable room."

The fact which is taken as proof of the existence of a vegetative cerebrospinal tract is the transitory suspension of the vasomotor reflex in complete transverse section of the spinal cord. This may be explained in the same way as the transitory suspension of the tendon reflexes and of the sphincter reflexes under the same circumstances, the explanation being a sudden fall in the tonic influences upon the spinal cord.

"If," says Müller, "we assume a center in the cortex for vasomotors, we must assume one also for the heart, stomach and intestines, and not only for their musculature but also for their glands, also for the genital organs, salivary glands, sweat glands and piloerectors, for all of these organs as well as the vasomotors are influenced by this or that change in emotional activity."

II. How may the effect of emotions upon the vegetative nervous system be explained in view of what has just been said about psycho-vegetative cortical centers? The physiologic effect of emotions is demonstrated every day. Blushing in shame, pallor, mydriasis and increased peristalsis in fright, tears in sorrow, gasping breathing in anger, palpitation in joy, sweating in anxiety, goose-flesh in fear, salivation resulting from appetite, urgency of urination in restless waiting, increase of sexual potency during good humor and diminution during bad humor, etc.

In the state of satisfaction the psychic reflex does not take place. Appetizing odors of food do not call forth salivation, nor do adequate stimuli bring forth sexual desire or erection, nor does a pistol shot accelerate the heart rate or bring forth sweat. The emotion as a product of a corresponding association is not physiologically produced under conditions of satisfaction.

The bodily manifestations of psychic occurrences are so constant in the vegetative domain that they have been used as precise measures in psychophysiological studies. The following reactions have been used: (*a*) Measurement of the pupil (Bumke), (*b*) measurement of the activity of the salivary glands (Pawlow), (*c*) measurement of the involuntary activity of the bladder (Mosso), (*d*) measurement of the skin resistance during various degrees of sweating (Veraguth's psychogalvanic reflex phenomenon), (*e*) measurement of the activity of the vasomotors and the heart (Mosso-Lehmann plethysmographic test of blood distribution).

The somatic manifestations of psychic occurrences are also of great significance in the consideration of psychophysical parallelism, a theoretical postulate which has received much attention in the modern study of brain physiology and psychology.

III. How may the influence of higher intellectual activities and emotions upon vegetative functions be explained?

The normal equilibrium of all centrifugal impulses, while it is constant, shows, according to H. Nusbaum, a correspondence to the state of our consciousness as well as to our objective appreciation of our own state. When the normal balance of centrifugal impulses is disturbed, something unusual has occurred and presents

itself to our Ego as such and gives us the objective picture of a change of feeling. Thanks to the centripetal nerves, the physiological condition of our organs is carried to those nerve centers which maintain a normal centripetal equilibrium. This balance of impulses as a constant, unchanging, normal relation does not enter consciousness but at most gives a vague feeling of its presence. "Only a change in this equilibrium stimulates consciousness and leads to excitation of the subjective element which we speak of as the feelings."

L. Müller proposes a very similar viewpoint which also quite denies any anatomical representation of the vegetative nervous system in the cerebral cortex or in centrifugal spinal tracts. He maintains that the biotonus or bioelectrical state of the brain and spinal cord undergoes a change when bodily pain, emotions or mental processes accompany a change in the feelings (the voluntary impulse, activity due to attention or to the act of representation). "Just as a barometer registers changes in air pressure which we cannot perceive, so do minute changes in volume of the blood in the vessels and the diameter of the pupil give indications of changes in the central nervous system which are in the main not perceived."

These delicate organs of precision are comparable to the objective of a microscope which magnifies the size of an object or to the multiplier of a galvanometer which magnifies the minute deviation of the magnetic needle.

The variations in biotonus show changes not only in the vegetative nervous system, but also in the psychomotor system (change of the intensity of the tendon reflex in attention, characteristic activities and thoughts in joy and depression).

It is also worthy of note that ganglion cells of various organs react to various kinds of emotional stimulation, tears in sorrow (ganglion lacrimale), heart ganglion in fright. Just as laughter brings the ganglion cells dominating certain facial muscles, the diaphragm and the vocal cords into activity without there being a laughter center, so do the by-effects of various emotional states bring about changes in various groups of the visceral ganglion cells of the midbrain, medulla and spinal cord. The visceral system, particularly the eye and facial blood vessels, may be regarded as a mirror of the soul upon which each psychic change is reflected.

The varying tonus of the vegetative nervous system dominated by external and internal influences is subject to some laws which all psychologists are agreed upon. In old age and in extreme fatigue the projection of psychic activities upon the vegetative nervous

system is diminished—sluggish pupil, diminished potency, mild blushing, slow warming and sweating of the skin. "It is hard to say in how far diminished activity of the emotions on one hand or diminished reactivity of the vegetative nervous system on the other are responsible. Probably both factors play a part" (Möller).

Further mention will be made of the interesting relations of psychic activities to vegetative activities in the chapter dealing with the relations of the glands of internal secretion and the vegetative nervous system.

CHAPTER VII

Pharmacology and Pharmacodynamics of the Vegetative System

Many factors enter into the maintenance of the activity of the vegetative nervous system. There are not only, as we have seen in the section on physiology, primary sensory stimuli from the periphery, and secondary stimuli through the feelings and the mental events taking place in the cerebrum, but also stimuli derived from a variety of chemical substances. These stimulate the vegetative system without affecting the cerebrospinal system, and may be classified:

I. As pharmacological preparations, or drugs.

II. As products of internal secretion, or hormones.

At this point the antagonism between the innervations of the sympathetic and autonomic systems, as briefly described above, becomes very important. One may justly conclude from the remarkable fact of the selective influence upon one or the other system, of the above named classes of substances, that the cells of origin, and the peripheral endings of the mesencephalic, bulbar and sacral autonomic fibers differ essentially in their chemical affinity from those in the sympathetic system. We shall commence with a discussion of the exogenous substances, considered in connection with the fundamental experiments of the Vienna School, with the exhaustive pharmacological review of Fröhlich, the classical work of Biedl upon internal secretions and the control experiments of Petrén and Thorling, Bauer and Aschner. Later, we shall consider the endogenous substances or "hormones."

I. The first place among exogenous substances belongs to nicotine. This drug has played an exceedingly important rôle in the history of the physiology of the sympathetic nervous system. Pharmacological experiments with it have yielded valuable and fundamental insight into the anatomical structure of the vegetative system. For this we are indebted to the fundamental experiments of Langley and Dickenson. They have taught us that the paths of vegetative nerves are not interrupted as are those of the motor nerves to voluntary muscle, but that the interpolation of a single ganglion cell makes a division into two neurones, and that this

division or interruption, the synapse, marks the transition between preganglionic and postganglionic segments. After intravenous injection of nicotine, or after brushing the ganglion with the alkaloid; stimulation which is precellular, or central to the synapse, is without action, while stimulation peripheral to the synapse, or retrocellular, that is of the second neurone, beginning in the aforementioned ganglion cell, and ending in some organ, does give a reaction. It is obvious that by means of a one per cent. nicotine solution one may also determine the place of interruption in those cases in which the sympathetic fibers pass through several ganglia, and are only interrupted in one of them. For example, the pupilodilator fibers, which go through two ganglia, to be finally interrupted in the superior cervical ganglion, and the nerves to the intestine, which pass through several ganglia, before being interrupted in the coeliac ganglion.

Nicotine in strong concentration at first stimulates, later paralyzes. At first it acts upon the vasomotor and the sweat glands, and thereafter upon all the vegetative organs. During smoking the stimulating effect is in the foreground, and it is only exceptionally that human beings are severely poisoned by nicotine with the subsequent paralysis of the medullary-respiratory center, and of the vasomotor center, an effect which is readily obtained in animals. We may speak of nicotine as a vegetative katexotic poison, which influences all the ganglion cells of this system, both sympathetic and autonomic. On the other hand, the other, better known alkaloids, and the products of internal secretion act exclusively on one system, whose tone they alter, that is to say, they are either sympathicotonic, or autonomotonic. Since the autonomic system is mainly represented by the vagus, we speak of the last named group of substances as "vagotonic" substances.[1]

A. The exogenous substances which are of a vagotonic or vagotrophic nature, *i. e.,* substances which affect the activity of the mesencephalic bulbar and sacral divisions of the autonomic system, include

1. Poisons which paralyze the autonomic nerve endings, vagoparalysants; atropin and the nitrites. Atropin paralyzes the accelerator nerves (mydriasis, inhibition of sweating). Nitrites paralyze the inhibitory nerves (vasodilators of the N. erigens).

2. Poisons which stimulate the autonomic nerve endings, vago-

[1] Care must be exercised not to confuse *Vago-tonic* with *Vag-atonic* (its opposite), a term utilized by some. The latter term were better eliminated entirely as it is a source of confusion. *Vago-inhibitory* is suggested as a substitute. (Trans.)

spastics; muscarin, pilocarpin, picrotoxin, and physostygmine. The last mentioned is distinguished from the others by the fact that its action is less a stimulating one, and more one of raising the threshold of the sensitivity of the nerves. The physiologico-pharmacological manifestations of the action of these substances is decrease in blood pressure, weakening of cardiac action, bradycardia, narrowing of the pupil, increased glandular secretion, and spastic peristalsis in the gastro-intestinal tract.

It is noteworthy that it is only exceptionally that a substance has a universal action upon the autonomic system.[2] Most of them have a selective action. Atropin has a powerful influence upon the cranial branches, little upon the sacral branches, while the nitrates influence the latter in the main, but not the former.

Pilocarpin has a strong selective action upon the secretory fibers, while muscarin affects the cardiac fibers. We see the same kind of activity among the sympathicotonic poisons. The teleological significance of the two nervous systems obviously lies in the fact that they act antagonistically. So it is comprehensible, as the accompanying table by Fröhlich bears out, that, as is the case with nervous stimulation, so it is with the chemical stimulants affecting corresponding parts. They have an antagonistic action upon one another.

TABLE

	Central Stimulant	Peripheral Stimulants		Peripheral Paralysants		Augmenters of the Peripheral Irritability
		Accelerator	Inhibitor	Accelerator	Inhibitor	
Autonomic	Picrotoxin	Pilocarpin Cholin		Atropin	Nitrites	Physostygmin
Sympathetic	Beta-tetrahydronaphthylamin	Adrenalin	Adrenalin	Ergotoxin		Cocaine

B. Among the exogenous substances which are of a sympathicotonic or sympathicotropic nature, and which may change the irritability of the sympathetic system, may be mentioned:

1. Poisons which paralyze the sympathetic system—sympathicoparalysants, ergotoxin. It has a strong selective action, only paralyzing the accelerator nerve endings, and not the inhibitory nerve

[2] Morphine produces general diminution of function by paralyzing stimulatory and stimulating inhibitory fibers. This rule may be applied to either system as a whole. For confirmation compare the action of morphine with that of electrical stimulation of either system on page 60. Details will be found in an article to appear shortly in the Journal of Nervous and Mental Disease, by the translator. (Trans.) (July, 1918.)

endings, thus becoming a valuable agent for the discovery of the inhibitory sympathetic nerve fibers.

2. Poisons which stimulate the sympathetic system, sympathicospastics—ephedrin and tetrahydronaphthylamin. Ephedrin stimulates the peripheral nerve endings of the sympathetic system, particularly the smooth muscles of the eyeball (dilator muscle of the iris) and of the orbit (Müller's muscle), whereas tetrahydronaphthylamin stimulates simultaneously the central and peripheral parts of the sympathetic. So much for the exogenous poisons.

II. Of great biological significance are the pharmacological studies upon endogenous or endocrinous substances, studies which have already made a promising beginning in the clinic. These also it is advisable to separate into vagotonics and sympathicotonics.

A. Among the vagotonic substances which stimulate the autonomic system, cholin must be mentioned (oxethyltrimethylammonium hydroxide) which may be obtained in abundance from the cortex of the adrenals, and whose stimulating action upon the peripheral accelerator nerve endings of the autonomics is very similar to that of pilocarpin. It acts upon the vascular system and the pupil in antagonistic fashion to the other product of the adrenals, to be described below, namely adrenalin, which diffuses after death in large quantities from the medulla into the cortex, and which almost entirely inhibits the action of cholin.

B. Among the sympathicotonic substances must be mentioned the following: Iodothyrine, hypophysin and adrenalin. The first two stimulate parts of, the last, the entire sympathetic system. The products of the glands of internal secretion are called hormones when obtained chemically pure, that is to say they are substances of simpler structure than proteins, unaffected by heat, and diffusible through animal membranes. We shall merely mention here those products of internal secretion of the pancreas, of the mucous membrane of the stomach, and male and female sex glands. These are partly sympathicotropic, partly vagotropic, and up to this time have been but little studied.

I. Iodothyrine, or iodothyreoglobulin, the hormone which is gotten from the secretion of the thyroid gland, or from the thyroid gland itself, causes, when continually produced, a chronic condition of stimulation in the sympathetic (tachycardia, widening of the lid slits, exophthalmos, emaciation, sweating and increased sensitiveness of the eye to adrenalin). Its action is selective, in that it excites, or makes more excitable, only the cervical and thoracic sympathetics.

II. Hypophysin, pituitrin, or pituglandol, the active principle of the infundibulum hypophysi contracts all arteries (rise in blood pressure) with the exception of the renal vessels which are dilated (diuresis) and stimulates the lumbar sympathetics, especially the nerves to the bladder and uterus (action of stopping hemorrhage and stimulating labor pains). In larger doses it has some influence upon the autonomic system.

III. Adrenalin, or suprarenin, a methyl amino derivative of pyrocatechol which, unlike cholin, is *not* found in the cortex, but in the medulla of the adrenals, may be considered as the most important representative of that group of hormones which act upon peripheral nerve endings. It acts even though the connecting nerves, from the central nervous system, be divided. Since the entire action of adrenalin is present, even after the preganglionic and postganglionic fibers have been divided for months or years, the place of its action, as has been said before, is at that part of the nerve which does not degenerate after section of the nerve, that is the myoneural junction (Elliot).

Adrenalin, which may also be found in a slightly modified form in the aortic, carotid and coccygeal paraganglia, is by no means, as is sometimes falsely stated, a stimulant of smooth muscle. It stimulates the entire sympathetic, and produces in its accelerator nerves acceleration or increase in the functional activity of the organs which they supply, while in its inhibitory nerves, it produces inhibition or decrease of function.

The manifestations of its actions are as follows: Tachycardia, increase of cardiac action, increase of blood pressure through vasoconstriction, mydriasis and exophthalmos, depression and an anemic state in the respiratory and gastrointestinal tract, increase in sphincter tonus, and decrease of the secretions of various glands. It also affects carbohydrate metabolism, in that it has a mobilizing action upon the carbohydrate storehouses, the liver and muscles, which causes glycogen to be broken down, and increases the burning of sugar.[3] It also, by peripheral stimulation of the sympathetic, produces a transient glycosuria, in the same way as the central stimulation of the Claude Bernard "Piqûre."

The antagonistic action between the sympathicotropic adrenalin, and the vagotropic pilocarpin, both of which stimulate the accelerator nerves peripherally, is made clear by the facts that adrenalin abolishes pilocarpin eosinophilia, and that pilocarpin abolishes adre-

[3] *Tr. Note.*—Lusk has contended, on the basis of his experiments, that this is not so, and that carbohydrate and nitrogen metabolism are unchanged by injection of adrenalin.

nalin glycosuria. The antagonistic action between adrenalin and cholin, both hormones of the adrenals, is less outspoken.[4]

Of the internal secretions, that of the pancreas is the most sensitive to adrenalin. The production of adrenalin is normally inhibited by the pancreas, and is enormously increased after its extirpation. In congenital or inherited deficiency of the chromaffin system (Addison's disease) the actions of the autonomic system are in the foreground.

The following interesting facts are to be noted in regard to a peculiar antagonism in the influences which regulate the blood picture.

All sympathicotonic substances, by virtue of an intense stimulation of the bone marrow, produce a long-lasting neutrophil hyperleucocytosis, with an eosinophilia, while, on the other hand, all vagotonic substances produce a transitory retention of neutrophil cells in the internal organs, an absolute increase in the mononuclear cells, *i. e.,* lymphocytosis, and an outspoken hypereosinophilia.

The following facts will show how exactly alike are stimulation by adrenalin, and stimulation of sympathetic nerves.

I. Adrenalin stimulates all sympathetic fibers to blood vessels (vasoconstrictors) and produces a general narrowing in blood vessels, and an increase in blood pressure. The coronary arteries are the exception in having only vasodilators, and here a teleologically significant local dilation of the blood vessels results. Finally, adrenalin has no effect upon the blood vessels of the lungs, since they have no sympathetic innervation.

II. Many organs, as the bladder and uterus, which in different species of animals, dogs, cats and rabbits, are variously influenced by the sympathetic system, are also variously influenced by adrenalin. When stimulation of the nerves accelerates, adrenalin does also, whereas if the action be inhibitory that of adrenalin is the same.

The following observations may be drawn from our knowledge of the action of adrenalin. First: with the exception of glycosuria, all its actions are obtained more rapidly by intravenous than by subcutaneous injections, and, second: the action of repeated injections is lasting, whereas a single injection produces but transitory effects, though the blood still contains adrenalin and has the power of raising blood pressure when injected into other animals.

Whether the great depression of blood pressure, the rapid de-

[4] *Tr. Note.*—For the literature and discussion of the action of acetylcholin, see Gaskell.

crease of blood sugar and death resultant upon extirpation of the adrenals are due to some unknown auto-intoxication, or to a lack of adrenalin, has not as yet been decided. This is especially true when one considers that besides adrenalin (Wessely) the adrenals excrete the antagonistically acting cholin (Lohmann), as well as other hormones of physiological significance.

There is, beside the physiologically produced adrenalin, a synthetic adrenalin of identical biological and chemical characteristics. This is composed of levorotary, and dextrorotary components, and is optically inactive. It is not toxic, does not increase blood pressure, and diminishes the blood-raising power of adrenalin.

Before ending our consideration of the pharmacology of the vegetative system, and proceeding to the sections on general pathology, and clinical aspects, a word must be said about the experimental production of a state of increased reactivity in the organs supplied by the vegetative system. This condition may be obtained as well by isolation of the organs from the central nervous system as by the poisons above mentioned.

The phenomena, resultant upon isolation of the organs, may be demonstrated by extirpation of the sympathetic ganglia, with subsequent degeneration of the post-cellular fibers. In this experiment, the reactivity is very much increased. A minimal dose of adrenalin, which ordinarily would produce little or no effect, will cause, when injected intravenously or subcutaneously, a mydriasis and anemia of the ear of the operated side.

Among the drugs which raise the threshold of irritability, physostigmin has already been mentioned. This increases the irritability of the autonomic system. Cocaine has the same effect for the sympathetic. It so increases the irritability of the nerve endings in organs that a normally inactive dose of adrenalin will produce a marked and lasting reaction.

This increased irritability, when noted in the pupil, is designated as Loewi's reaction. It does not appear to be a general reaction, but occurs only in certain organs.

The explanation of this phenomenon is by no means clear. It may be a removal of inhibitory influences. Probably, it is due to the absence of centrifugal impulses from sympathetic end-organs, which aid in maintaining a certain level of tone in them. After the use of cocaine or section of afferent and efferent nerves, the normal inhibitory influences which diminish organ irritability are absent. Analogous phenomena occur in the case of the retina in absolute darkness and in the case of the labyrinth in absolute silence.

Action of Stimulation of the Sympathetic System	Action of		Organ	Action of		Action of Stimulation of the Autonomic System
	Atropin	Adrenalin		Pilocarpin	Ergotoxin	
———	Para.	———	Sphincter iridis	Stim.	———	Stim. (N. III)
Stim. (Th. I–II)	———	Stim.	Dilator iridis	———	———	———
———	Para.	———	Ciliary muscle	Stim.	———	Stim. (N. III)
Stim. (Th. I–III)	———	Stim.	Orbital muscle	Para.	Para.	———
———	Para.	(Stim. ?)	Salivary glands	Stim.	———	Ch. tympani. secretion
Stim. (Th. II–IV)	———	Constriction	Cortical blood vessels	———	———	Dilatat. (N. X)
———	———	Dilatation	Buccal blood vessels	———	———	Constrict. (N. IX)
Constrict. (Th. II–IV)	Constrict. ?	Constriction	Skin blood vessels, head region	———	———	———
———	Dilatation	Dilatation	Coronary blood vessels	Constrict.	———	———
Constrict. (Th. II–L. IV)	———	Constriction	Intestinal blood vessels	———	Dilatat.	———
Constrict. (L. I–IV)	———	Constriction	Genital blood vessels	———	———	Dilatat. (N. pelv.)
Stim. (Th. II–L. IV)	Inhib.	Inhib.	Sweat glands	Stim.	———	———
Stim. (Th. IV–VII)	———	Stim.	Pilomotor muscles of the face	———	Para.	———
Stim. (Th. I–V)	Stim.	Stim.	Heart muscle	Inhib.	Inhib.	Inhib. (N. X)
Relax. (Th. II–V)	Relax.	Relax.	Esophagus	Stim.	———	Stim. (N. X)
Para. (Th. II–L. IV)	Para.	Para.	Cardia	Stim.	———	Stim. (N. X)
Diminished (Th. II–L. IV)	Diminished	———	Gastric tone	Increase	———	Increases (N. X)
Para. (Th. II–L. IV)	Para.	Para.	Gastric peristalsis	Increase	———	Increases (N. X)
Diminished ?	Diminished	Diminished ?	Gastric secretion	Increase	———	Increases (N. X)
Inhibition (Th. II–L. IV)	Para.	Para.	Small intestine peristalsis	Stim.	———	Stim. (N. X)
Relax. (L. I–IV)	Relax.	Relax.	Colon	Stim.	———	Stim. (N. pelvicus)
Relax. (L. I–IV)	Relax.	Relax.	Sphincter ani (muscle)	Spasm	———	Spasm (N. pelvicus)
Relax. (Th. II–L. IV)	Relax.	Relax.	Gall-bladder	Contract.	———	Contract. (N. X)
Inhib. ?	Inhib.	Inhib.	Pancreatic secretion	Stim.	———	Stim. (N. X)
———	Inhib.	Inhib.	Bronchial muscle	Stim.	———	Stim. (N. X)
Contract. (L. I–IV)	———	Contract.	Sphincter vesicæ	———	———	Relax. (N. pelv.)
Relax. (L. I–IV)	———	Relax.	Detrusor vesicæ	———	———	Contract. (N. pelv.)
———	———	Contract.	Uterus (Preg.)	Relax.	———	———
———	———	Relax.	Uterus (Non-preg.)	Contract.	———	———
Contract. (L. I–IV)	———	Contract.	M. retractor penis	———	———	Relax. (N. pelv.)
Piqûre	———	Raised	Carbohydrate tolerance	Diminished	———	———
Heat puncture	———	Raised	Heat balance	———	———	———
Contract.	———	Contract.	Pigment cells	Dilatat.	———	———

Stim. = stimulation. Constrict. = constriction. Relax. = relaxation. Para. = paralysis. Inhib. = inhibition.

This peculiar action of cocaine is of practical value, since, in cases where the results of large injections of physiological adrenalin or the less toxic synthetic adrenalin are to be feared, a dose of cocaine may be given which will increase the action of the adrenalin.

At the close of this consideration of the pharmacology of the vegetative system, we have placed a table which contains a résumé of the actions of the better known substances which influence the autonomic and sympathetic systems. This table has been compiled from the works of Eppinger and Hess, A. Biedl, Fröhlich, and Loewi.

CHAPTER VIII

General Pathology of the Vegetative System

During the last few years the Vienna school have attempted to show that the idea of sympathicotonia and vagotonia is not only applicable in experimental physiology and pharmacology, but that it may be applied in the clinic as well. Observation teaches us that the phenomena which may be demonstrated in experimental work are the same as those which appear as symptoms and symptom complexes at the sick bed. One must, however, in addition to such observations attempt to make clear what metabolic changes are taking place in the body, and where, in a given case, the body toxic poisons are acting, or to put it more generally, we must, in addition to noting symptoms and symptom complexes, attempt to find the etiology.

Physiology teaches us that after the nerves to many smooth muscles are cut, the tonus of these muscles returns in a short time. From this we may deduce that the muscles have intrinsic nervous organs which maintain their tone, and that the sympathetic and vagus act only as inhibitory or stimulatory influences upon the ganglion residing in the muscle.

That the fibers of the vagi are in a state of continuous tonus, is best shown by the fact that bilateral bisection of these nerves causes a permanent acceleration of the heart beat.

As to the tonus of the sympathetic nerves to those organs, cutting the peripheral sympathetic gives, among other phenomena, narrowing of the pupil, exophthalmus, and a dilatation of the blood vessels softening the glands and the skin of the face.

Aside from the data derived from the last named nerves, we know that the endogenous sympathicotropic hormone, adrenalin, which stimulates the sympathetic system, is continually being formed by the chromaffin cells of the body and that in this way the tonus of the sympathetic system is, in all probability, kept permanent.

Less constant is the action of the products of the thyroid and infundibulum of the hypophysis, two of the group of glands which stimulate the sympathetic, and the action of the parathyroids, pancreas and ovaries, which are of the sympathetic inhibiting group.

Whether or not the body produces a vagotropic hormone action, as pilocarpin, is not known. Most of the vagotropic products (cholin) are produced in small amounts and are known to have an elective action upon the autonomic system. One fact, clinically verified by a large number of cases, is certain; that individuals whose reaction to adrenalin is increased beyond the normal, show underactivity towards pilocarpin.[1]

One may, therefore, state that a given individual is of a vagotonic constitution when, together with functionally increased tonus of the vagal system, there exists an increased reactivity to vagotonic substances (pilocarpin). There are individuals in whom the manifestations of activity of the sympathetic system predominate. These react more strongly than the normal to adrenalin. And on the other hand there are those in whom the manifestations of activity of the autonomic system predominate. These react much more strongly than the normal to pilocarpin. Following this idea, the functional activity of the vegetative system is tested by drugs acting either upon the autonomic or sympathetic system. Resultant upon our knowledge of pharmodynamic antagonism, a method has been devised by which to make clear the clinical picture of the supposedly frequent condition of vagotonia.[2]

How does the symptom-complex of vagotonia manifest itself clinically? The physiological signs of stimulation of the autonomic system have been described in detail above, and all of these are reproduced in the clinic: Narrow pupil and spasm of accommodation (stimulation of the sphincter and of the ciliary muscle of the pupil), widening of the lid slits (stimulation of the levator palpebræ), salivation and epiphora (stimulation of the chorda tympani and of the lacrimal nerve), hyperidrosis (stimulation of the sweat nerves), reddening of the face and mild cyanosis of the sweating extremities (stimulation of the vasodilators), strong pulsation of the heart, bradycardia, pulsus irregulatorius respiratorius, disturbance of the propagation of the cardiac impulse, phrenodynia, temporary cessation of breathing (stimulation of the branches of the vagus going to the heart and lungs), bronchial asthma (stimulation of the smooth musculature of the bronchi), eosinophilia, hyperacidity, increased gastric peristalsis, transitory spastic conditions in the esophagus, cardiac and pyloric musculature, tonic contracture of the intestine, spasm of the musculature of the gall bladder and of the pancreatic duct (stimulation of the abdominal vagus), spasm of the circular muscles of the colon, of the sphincter anus muscle,

[1] *Tr. Note.*—This is not always the case.

[2] See "Vagotonia," Monograph Series No. 21.

of the detrusor muscle of the bladder, and of the vasodilator muscles of the bladder and genitals (stimulation of the pelvic nerve). All of these phenomena are said to disappear after large doses of atropin and to increase after pilocarpin.

Eppinger and Hess include among the vagotonic neuroses of the heart: Vasomotor angina pectoris (stimulation of the vasoconstrictors of the coronary vessels) Hertz's bradycardiac hypotonia and the phrenocardia of sexual origin.

B. Vagotonia regarded as a functional disease of the autonomic system may, according to the above mentioned authors, present itself as a malady which may be general or local, individual or familial, permanent or periodic, pure or combined, adult or juvenile, outspoken or abortive, manifest or latent.

Local vagotonia is the functional increase in tonus which results from toxic substances, circulating in the organism, which have a selective action upon definite autonomic nerves (the nerve to the sphincter muscle of the pupil, the vague nerve or the pelvic nerve). Periodic vagotonia manifests itself particularly as local cardiospasm or esophageal spasm, or as a functional heart disease. Combined vagotonia shows the pure symptom-complex plus such conditions as enteroptosis, cor mobile, pendant heart, costa fluctuations, persistent thymus, lymphatism, status thymico lymphaticus (Paltauf), eunuchoidism (Tandler-Gross), mongoloid degeneration, asthmatic constitution (Stiller), hypoplastic and other constitution anomalies which, as vagotonia itself, are regarded as evidence of inferiority and degeneration.

The question now arises, how may one establish a diagnosis of vagotonia, or of a vagotonic disposition? We understand the clinical picture of vagotonia to be a permanent, tonic over-activity in the autonomic system, by virtue of which the organs supplied by it are in a condition which closely corresponds to that which would be produced by stimulation of the autonomic system. This condition must be considered as the basis of the vagotonic disposition, *i. e.*, "an abnormal reactivity of the entire or of only a definite part of the autonomic nerves, which under the influence of an adequate stimulus will lead, even if this stimulus be of less intensity than one to which the normal nervous system would react, to the syndrome of vagotonia" (Eppinger and Hess).

Vagotonia occurs chiefly in youthful or middle-aged individuals who are particularly subject to autonomic traumata, and who show, either permanently or transiently, one or more of the manifestations described above.

When vagotonia is suspected, a subcutaneous injection of pilocarpin will reveal the existence of vagotonic symptoms which may give rise to no complaints on the part of the patient, or may metamorphose serious latent pathological disturbances into manifestly acute conditions, such as tabetic crises, bronchial asthma, bradycardia, or angina pectoris vasomotorius.

In other cases, the appearance of a suspected symptom in some branch of the autonomic system (as a crisis or salivation, for example) may be accompanied by more symptoms, as for example miosis, epiphora or goose flesh, which are readily recognizable and are to be regarded as manifestations of over-activity in other branches of the same system.

Atropin and often adrenalin affect the symptoms and signs of over-activity of the autonomic system favorably, pilocarpin unfavorably. To bring this out, the optimum dose in man, subcutaneously administered, is

Atropin	1 mg. (gr. 1/70)
Pilocarpin	1 cg. (gr. 1/7)
Adrenalin	1 c.c. (♏ xv)

In advanced age, the reactivity decreases and vagotonia gets better, or may even disappear.

C. How are we to understand the genesis of vagotonia? Most probably, some product of internal secretion is the cause of the increased tone in the autonomic system. It is known that of the endocrinous products, of which more was said in detail above, adrenalin is an intense general stimulant of the sympathetic system, while thyroidin and infundibulin impart some vagotropic and some sympathicotropic impulses, while the secretion of the pancreas, and cholin derived from the cortex of the adrenals are purely vagotonic. The two last mentioned do not influence the entire autonomic system, but have a selective action. The internal secretion of the pancreas acts principally upon metabolism, while cholin acts chiefly upon blood pressure and the pupil. If one considers further what large amounts of the last mentioned substances would be necessary to maintain a permanent tonus in the whole system, it would seem, quite contrary to the case of adrenalin, very improbable that these bodies play the physiological rôle of the sought-for "autonomin" or "autonomic vagotonin."

Eppinger and Hess are of the opinion that vagotonia, like status lymphaticus and thymicus with which it is so often combined, is a partial manifestation of an inferior organism. Just as other organs and systems may be backward in their development, so also the

chromaffin system may be poorly developed, and thus less of the sympathicotonic adrenalin is produced, so that its antagonists may give more stimulation than when the activity of the medulla of the adrenals is normal.

Besides this congenital insufficiency and inferiority of the internal secretion in the realm of the chromaffin system, the Vienna School maintained the possibility of another condition which would be the basis of a so-called inherited constitution.

On the evidence of the parallelism, both clinical and at autopsy, between vagotonia and status thymicolymphaticus, they maintain that vagotonia may be the clinical manifestation of the anatomically demonstrable lymphatic constitution, and of the functional overproduction of the internal secretion of the lymphatic system. This is quite in accord with the fact that vagotonia appears mainly in youth, in which the lymphatic constitution is generally found. Furthermore, lymphatism and persistent thymus not infrequently coëxist with defects in the adrenals in which the chromaffin substance is lost.

In regard to the bearing of many physiological and pathological conditions upon vagotonia, the following may, according to the above-mentioned authors, be mentioned in addition to what has already been stated.

The climacteric, with its well-known vasomotor, secretory and metabolic changes (obesity) is an inherited vagotonic condition, which results from the removal of a sympathicotonic internal secretion. It is not out of the question that, in men also, the removal of a sympathicotonic internal secretion of the male genital organs (Mendel) may aid in giving autonomic stimuli in the climacteric age.

The clinical picture of Graves' disease and of myxedema is so fundamentally varied and contradictory that the thyroid product, according to the individual tendency of the patient, may stimulate the autonomic system (widened eye slits, von Graefe's sign, tachycardia, sweating, salivation, diarrhea and eosinophilia), or may stimulate the sympathetic system. In individuals without any outspoken tendency, the thyroid product produces symptoms in both systems, quite differently than in pure vagotonic or sympathicotonic individuals. In the present state of the matter, it is difficult to make a definite decision in regard to the peculiar experience, confirmed by Noorden, that pure Graves' disease is rarely, while mixed Graves' disease is always associated with psychopathological conditions.

It has been shown experimentally (Fleischmann) that thyroid

extract has a detoxifying action upon atropin, which may be easily shown on the heart which has been stimulated to stoppage by muscarin.

The chemical nature of the substance which stimulates the nerves and metabolism in Graves' disease is a thyreoiodo-globulin (Oswald, Gottlieb). The manifestations of stimulation of the sympathetic system, which may be designated "adrenalin symptoms," point to a sensitization of definite sympathetic structures for the action of the adrenalin which is always present in the blood. Thyreoiodo-globulin would therefore, analogously to cocaine, increase the irritability of the sympathetic nerve endings towards an adequate stimulation by the hormone of the adrenals.

While, in one instance, the vagotonic tendency may be the basis for a definite neurosis, in another it may modify in a definite fashion the progress of various organic diseases of the body. This applies to the relatively infrequent cases of tabes dorsalis where at the very onset visceral disturbances or crises (hypersecretion, increased peristalsis, sweating, epiphora, incontinence of feces, etc.) are in the foreground. It is precisely these patients who have a preëxisting vagotonic condition.

The prettiest example of a slowly developing vagotonia is Addison's disease, a condition from which general pathology has made many observations. In this disease, it is a question of a picture (emaciation, diarrhea, low blood pressure, hypoglycemia) whose origin lies in the disappearance of those organs from which spring the most important excitor of sympathetic impulses.

Early tuberculosis strongly recalls, both in its beginning symptoms and in the accompanying lymphatism, the Addisonian disease, since the chromaffin system, which in Addison's disease is found to be entirely destroyed, is damaged electively by the tuberculosis endotoxin.

Among the dermatoses, vasomotor urticaria and Czerny's infantile exudative diathesis appear in individuals, or in families with vagotonic tendency.

In mental diseases as well, the observations of Pötzel, Eppinger and Hess have shown that at the height of a severe psychic disturbance the equilibrium of the visceral nervous system is destroyed. The pharmacodynamic reactions of the autonomic and sympathetic systems to specific drugs is characteristically changed during psychic diseases (climacteric melancholia, manic-depressive insanity). Pötzl's cases of catatonia were carefully studied in this connection. In the acute cases, Rheinhard's cortical edema was found, which

Pötzl regards as probably due to stimulation of the autonomic nerves to the choroid plexus. This episodic over-reactivity of the vagus system of catatonics is partly a tendency, partly the disease itself, and recalls many of the conditions in the reaction of anaphylaxis.

In many sympathicotonic individuals, adrenalin glycosuria, or adrenalin mydriasis (Loewi's reaction) occurs.

What may yet be said in regard to the discussion of the pharmacodynamics and of the pharmacology of the vegetative system in regard to the question of the interrelations between the sympathetic and the glands of internal secretion, and in regard to that action of the glands of internal secretion upon the psychic functions?

The degree of emotional reactivity is of course not only influenced by the activeness of the mental state, and by the reactiveness of the vegetative system, but also by the quantity and quality of the products of the glands of internal secretion, which directly or indirectly, by means of their action upon the sympathetic system, influence the psychic functions.

What has been heretofore said yields, in the light of Munzer's summary of the subject, the following conclusions: The pathological changes of the secretions of many endocrinous glands—thyroid, pineal, hypophysis, sex glands—cause definite psychic manifestations (as for instance in Graves' disease, myxedema, acromegaly, castration) which lie essentially in the realm of affective life. A series of physiological conditions, among which puberty, pregnancy, menstruation, and old age may be mentioned, are frequently accompanied by a modification of the affective process, and at the same time, by an alteration of the normal secretions, of some glands (sex glands and thyroid gland). Definite diseases which are intimately related to the condition of increased or decreased secretion of endocrinous glands not infrequently follow directly upon violent emotions. The objective signs of some emotional excitements (palpitation of the heart, sweating, mydriasis) are equivalent to a complex of symptoms as we see them shown in dysglandulism, as for example in Graves' disease, Addison's disease and eunuchoidism.

However we may think of the significance of the glands of internal secretion as etiological agents, the fact still remains that, on the basis of clinical observations, the influence of many of the products of internal secretions upon the manifestations of the affective life are undeniably established. But now a new difficulty arises: to appreciate as a real fact the causal relation between internal secretions and cortical activity. Even though to-day the old theory of the sympathetic is placed in the background in favor

of other hypotheses, yet the fact of the close relationship between the glands of internal secretion and the sympathetic remains unchanged.

Many suppositions have been made concerning the mutual relationship of nerves and glands of internal secretion. Definite conclusions fail us. It has, however, frequently been pointed out that as the glands of internal secretion influence the sympathetic system, so, conversely, the sympathetic influences the glands of internal secretion. It has not yet been settled which of these two actions is the leader, nor to what degree one of the two serves to determine the function of the other. Most of the glands of internal secretion have a marked affinity for the central nervous system, as the psychoses of Graves' disease, acromegaly, diabetes, tetany, and Addison's disease show. This correlation, this relation one to another seems, as Münzer brings out, like that between two glands of internal secretion. When, as Münzer points out, two organs or organ groups, as the brain on the one hand and the polyglandular system on the other, are closely related, and obviousy influence each other, there must be some similarity in the mechanism of their functions. "Just as the polyglandular system is influenced by products from the glands of internal secretion circulating in the blood, so there may be internal secretions produced by the central nervous system which regulate the action of definite cerebral functions."

As to the etiological significance of psychic traumata in diseases of the internal secretions, the clinical observations tell us that diseases which are definitely internal secretory in nature (Graves', acromegaly) may develop after such traumata. On the basis of these observations, Münzer believes that he may conclusively state that, in a certain number of these cases, the original injury is of cerebral origin, while the lesion in the glands of internal secretion is of secondary nature.

Physiological relations: From these statements, the theory that the glands of metabolism and internal secretion most probably have projection centers in the cortex presents itself. It is at all events for the future to demand, by means of experimentally obtained, intense emotional conditions in animals, as well as by autochthonous human mental diseases, a definite anatomic study of the endocrinous organs, including the secretory cerebral choroid plexus, and the sympathetic nervous system. D. Bauer, relying on the researches and experiments of Katzenstein, Exner, Asher, and Fleck, and especially Weiner, has attempted to place on a firm basis the group

of diseases designated the neurosis of the glands of internal secretion on a firm basis. He states, reasoning from logical arguments, that, in conditions of general over-irritability and increased reactivity of the vegetative system, the secretory fibers to individual glands (the lachrymal, the nerves of the thyroid, the splanchnic nerves to the adrenals) are primarily stimulated and that thus this condition of increased tone in the sympathetic system may be followed by increased function in the organs which it supplies.

Since the endocrinous glands regulate the tonus of the nervous system, which, together with the general mixture of tissue juices, is known to be the active principle of that which we know as the constitution of the organism, we may be permitted to separate the neurosis of the glands of internal secretion from other organic neuroses.

They make up the transition between constitution and disease, and what at one time expresses itself as being a constitutional peculiarity may at another time, quantitatively increased and with an acute onset, present itself as a severe illness. Bauer's train of ideas is, as we see, in the main in agreement with that of Eppinger and Hess who speak of a vagotonic disposition of the organism, and a vagotonia, a disease.

The same holds good, on the whole, of other organic neuroses—heart neuroses, vascular, ocular, intestinal, respiratory and sexual neuroses—which may easily arise in individuals with a general increased reactivity of the vegetative nervous system, when an organ or group of organs is truly exceptionally vulnerable and reactive, or when a locus minoris resistentiæ has resulted from some previous organic disease with consequent related involvement of the same, and related psychic manifestations.

The justification of the existence of the conception of vagotonia and sympathicotonia has been repeatedly tested during the last few years. The most important question may, in my opinion, be stated as follows: May clinical medicine expect anything of practical worth from the newly, but not firmly established physiological conception, and from the pharmodynamic examination of the vegetative nervous system in their relations to conditions of tone in the body?

A synthesis has been accomplished in defining the disease picture of vagotonia which is undoubtedly ingenious and stimulating, even though it is undoubtedly a somewhat forced schematization and has not been confirmed by all the researches upon it.

The most fruitful thing in contemplating the whole subject lies in the great significance of hormones in the development of somato-neuroses in the various systems of organs. It is a question, in organic neuroses, bronchial asthma, gastric neurosis, mucus colitis, phrenocardia, vascular crises, sympathetic neuralgia, etc., of a disturbance in the neuro-dynamics of the innervators of the various organs, whether this be brought on by a disturbance of metabolism or by some other stimulation of the nervous system.

As we have seen from the previous general data (the special pathology follows below) we have here an almost entirely new and yet untouched field of investigation which may simplify our estimate of many pathological conditions which it has been customary to describe falsely as special forms of disease.

This new branch of neuro-pathology, visceral pathology, may perhaps, as is usual, lead to hasty or schematic conclusions, since the clinical material by which the clinical facts were established has not been any too large. It now becomes the duty of experimental pharmacology to investigate diseased conditions in relation to clinical observation, and to clarify both normal and pathologically altered functions of organs. The drugs are like tuning keys by which we may tighten a string in that complicated string instrument, the organism, in order to increase its vibrations, or on the other hand to loosen it in order to decrease its activity.

It now becomes a question of whether the clinical observations and the results of the tests of function really confirm the assertions about the functional system diseases of the antonomic system, particularly in the case of the diametrically opposed conditions of the two fundamental conceptions (autonomic and sympathetic). The material examined thus far has, as is usual in nosology when new syndromes spring up, shown that the conception of vagotonia is capable of much expansion, that it shows many exceptions to the rule, that all cannot be brought in line with the pharmacological scheme, that the selectiveness of certain hormones is limited and that mixed and transitional forms between the two main groups (autonomic and sympathetic) are not lacking. In brief, the two conceptions are passing through the same evolution, as for example tabes, multiple sclerosis, Graves' disease, paralysis agitans which to-day may be diagnosed without any of the etiological, pathognomonic or so-called cardinal clinical symptoms of their discoverers.

The theoretically exact and carefully worked out antagonism between the two groups may be regarded as an excellent schema which, however, cannot invariably be put to a practical application

Even if it be beyond doubt, says Bauer, that there exists a functional antagonism between the sympathetic system in its narrow sense, and the remaining anatomic system (the autonomic), and even if the two may be separated in their development, it must yet be emphatically stated that the systems worked out from physiology and anatomy are not entirely identical to those based upon pharmacological actions, and that the antagonism between sympathetic and autonomic does not appear the same physiologically as it does pharmacologically. The selectivity, the selective tropism of drugs upon the vegetative system demands restriction. In the same way: as pharmacodynamic testing of function does not affect all parts of the vegetative system equally, but brings out the wide dissociation of the individual actions of the neurotropic substances, so also does the physiological, mainly tonic, innervation fail to bring out increased reactibility in all parts supplied by the vegetative system, but manifests itself in the most widely varying combinations.

Other investigators have expressed analogous opinions (Falta, Newburgh, Nobel, Petrén and Thorling).

Bauer believes that there is but one recurring physiological condition which may truly be called vagotonic, namely sleep. It is characterized "par excellence" in a condition of over-activity of the autonomic system—narrowed pupils, slow pulse, tendency to sweat and to pollutions, attacks of asthma, colic-like attacks, crises of labor pains. "The fundamental basis of this phenomenon ('Night is the time of smooth muscles'—Schmidt) is," Bauer concludes, "as yet unexplained."

In my opinion, the vagotonia of sleep is to be explained in the main by the fact that the cross-striated musculature is at rest and the blood goes more to the unstriped muscle which, being better nourished, functions more actively.

Bauer advises justly when he urges that the investigation of the conception of vagotonia by drugs should be amplified and controlled by mechanical and physical procedures.

The most important and best known mechanical and physical methods of investigating functions are those which will be described in the special part in connection with the heart, lungs, vasomotors and sweat glands, and which include the demonstration of dermographismus, pulsus irregularis respiratorius, Aschner's reflex from pressure on the eyeball, Czermak's vagus pressure phenomenon, Erben's pulse phenomenon, and Veraguth's sweat phenomenon.

The best pharmacodynamic method of investigating function is

by means of adrenalin, atropin and pilocarpin. The investigation should be planned methodically, as follows:

A. Conjunctival installation and subcutaneous injection of 1 per cent. adrenalin.

B. Subcutaneous injection of adrenalin $\frac{1}{10,000}$ for every kilogram (2 2/10 lbs.) of body weight three hours after the ingestion of 100 grams of grape sugar, in order to determine the tolerance for dextrose.

C. Injection of atropin sulphate $\frac{1}{10,000}$ for every kilogram (2 2/10 lbs.) of body weight, to test the autonomic system.

D. Injection of pilocarpin hydrochloride $\frac{1}{1,000}$ per kilogram (2.2 lbs.) to test the autonomic system.

The original investigations of Eppinger and Hess were carried out with smaller doses, pilocarpin 0.01 (gr. 1/6), atropin 0.001 (1/64 gr.) and gm. 0.001 of adrenalin. The later investigations of Petrén and Thorling and of Bauer were carried out with still smaller doses; pilocarpin gr. 1/6–1/12, atropin gr. 1/128 and adrenalin gr. 1/64–1/128.

CHAPTER IX

Special Pathology and Clinical Aspect of the Vegetative Nervous System

The most important points in the special semiology of the various organs supplied by the vegetative system will be discussed, in so far as they are of anatomico-pathological and clinical significance. Since it is undeniable that rational diagnostics are built up upon the facts of pathological physiology, a short résumé of the physiology, particularly in its newest aspects, based particularly upon the facts in the sections of general physiology, will head each section.

1. *Eye.*—The eye contains a considerably large number of vegetative organs—the ciliary muscle, the sphincter muscle of the iris, the dilator of the iris, Müller's orbital muscle, smooth muscles in the eyelids and the lachrymal glands. Some of these are supplied by the autonomic, and some by the sympathetic nervous system. The innervation of the pupil plays a very important rôle.

The question of the spinal and mesencephalic origins of the pupillary nerve fibers, of their sub-cortical tracts and cortical centers, of the ganglia and communicating branches, as well as of the antagonistic actions on the part of the autonomic on the one hand, and the sympathetic on the other, has been a matter of controversy for decades.

What share do the sympathetic nerves take in the innervation of the eye? It is known that the origin or nucleus of the pupillary dilator fibers lies in the spinal cord at the level of the 1–3 thoracic segments (the cilio-spinal center of Budge). From this origin, the fibers pass by way of the white rami communicantes to the cervical sympathetic cord, through the lower cervical ganglion to the superior cervical ganglion where they are interrupted and pass as post-ganglionic gray fibers to the Gasserian ganglion. Here they join the first branch of the trigeminus, and pass in the long ciliary nerves to the orbit to supply its floor vessels as well as the dilator pupillæ and Müller's muscle. This latter muscle, by its contraction, forces the eyeball forward.

We gain information as to the other central paths of the sympathetic pupillary fibers from the experimental work of Karplus and Kreidl. Electrical stimulation of a definite place in the floor of the mid brain, beyond the optic tract and lateral to the infundibulum,

causes in cats a reaction of the sympathetic fibers. There results maximal dilation of the pupil, widening of the lid slits, retraction of the internal aspect of the lids, as well as reactions in the sweat glands and bladder. The stimulation acts upon the homolateral side of the brain and sends impulses down the cord which cross over in part and stimulate Budge's center bilaterally, thus sending stimuli up both sympathetic cords.

It is doubtful whether it be necessary to assume, in addition to the thoracic and midbrain centers already described, the existence of a higher bulbar cilio-spinal sympathetic center as Roux, Paviot and Cordier state. Sympathetic paralysis in bulbar and cervico-thoracic lesions, nuclear and paranuclear, amply explain the centers above described. Whether indeed the cilio-spinal center be a completely coördinated center, only serving, as Roux would have it, pupillary reactions to skin stimuli, must remain an open question.

If we now consider the second class of innervation of the eye, we find the nerve to be the autonomic part of the oculomotorius and that its vertebral ganglion is the ciliary ganglion.

This latter is not a mixed ganglion with both spinal and sympathetic cells, but is a purely vegetative, autonomic ganglion, It contains absolutely no spinal cell elements, all the cells, according to L. Müller, being unipolar, hook shaped and encapsulated, with short dendrites. In spite of the vegetative nature of this ganglion, its histological appearance differs from that of the prevertebral abdominal ganglia, and the sympathetic cord ganglia in that the cells of these latter are not encapsulated, and have long dendrites.

The oculomotor nerve can only influence the smooth muscle of the iris through its autonomic ganglion, since its other fibers are solely for the supply of cross-striated muscle.

The following are the connecting tracts to the cerebrospinal axis and to the organs innervated. The pre-ganglionic fibers (ramus albus) are those which go from the oculomotor to the ganglion (radix brevis G. ciliaris). There is no agreement as to the origin of these particular fibers to the ciliary muscle and the sphincter of the iris. The intactness of the intrinsic ocular muscles in muscular atrophy, chronic ophthalmoplegia, poliomyelitis, and polyneuritis, in spite of the injury to the extrinsic muscles, speaks for a difference in clinical behavior, anatomical localization, and physiological type of the nuclei in the central nervous system, differences which have long been considered analogous to those existing in the corresponding centers for smooth and cross-striated muscle in the spinal gray matter.

According to Tsuchida and Monakow the innervation of the pupil is controlled by the small ganglion cells at the anterior end of the main lateral nucleus of the oculomotor. These cells are hard to separate from those of the neighboring Edinger-Westphal nucleus as Bernheimer localizes it. The sphincter nucleus is at any rate to be sought for in the gray matter ventral to the third ventricle. The oculomotor fibers of the radix brevis of the ciliary ganglion are interrupted in the ciliary ganglion and become the ramus griseus and as the short ciliary nerves pass into the inside of the eye and to its smooth musculature. It must be added that these ciliary nerves in spite of being postganglionic occasionally have a thin sheath and on entering the ciliary muscle form a fine ganglionic plexus.

The ciliary muscle or muscle of accommodation, whose center lies at the anterior medial nucleus of the oculomotor group, also receives fibers by way of the ciliary ganglion. After being interrupted here they become short ciliary nerves and pass on to their end organ.

There are two communicating branches of the ciliary ganglion which are of comparative anatomic interest and will receive attention here. The first branch is comparable to the fiber which passes from the sympathetic chain ganglia to the posterior spinal ganglia and thence to the sensory root. There is a delicate sensory root, radix longa, which passes from the nasociliary branch of the trigeminal nerve to the ciliary ganglion. We are still uncertain whether these fibers end in the ganglion or pass further, nor do we know the significance or function of these sensory fibers. Experiments in which the ciliary ganglion has been removed show that these fibers have no relation to sensation in the eye. There is an equal uncertainty surrounding a second branch which, as we shall see later, is of considerable diagnostic significance. This is the radix sympathetica of the ciliary ganglion, a branch of the sympathetic plexus ophthalmica which envelops the ophthalmic artery and arises in the carotid plexus. It is significant that in this way the sympathetic and its upper cervical ganglion which sends fibers to the dilator pupillæ comes into contact with the autonomic which sends fibers to the sphincter pupillæ through the ciliary ganglion. Analogous conditions occur in other cranial ganglia as well as in the ganglia of the sympathetic chain which supply the neighboring blood vessels with postcellular sheathless fibers.

The smooth musculature of the eye and orbit is supplied by two widely separated ganglia lying in two quite different localities of the cerebrospinal axis of the archipallium, *i. e.*, from the region of the

mesencephalic corpora quadrigemina and from the upper region of the thoracic spinal cord.

The tract from the corpora quadrigemina by way of the oculomotor nerve causes the pupil to react to light, accommodation and convergence by narrowing. The spinal sympathetic tract causes dilatation of the pupil, widening of the lid slits and slight forward protrusion of the eyeball. The antagonistic action of the two systems, which holds for all vegetative end organs, is present in the eye and is not only physiologically but also pharmacologically demonstrable. This latter is shown by the action of atropin upon the sphincter and accommodation muscles and of cocain upon the dilator muscle.

Two parts of the pupillary fibers remain for discussion, the retinonuclear and the corticonuclear, and there is much discussion between physiologists and clinicians concerning these.

The retinonuclear tract reminds one of the sensory part of the simple reflex arc. In all parts of the nervous system the sensory arc carries the stimulus inward to the neighborhood of a motor nucleus. Here it transmits it to the motor nucleus by means of collaterals. These are very sensitive to injury by one means or another, as the loss of the Achilles, patellar or corneal reflexes in tabes, polyneuritis or increased intracranial pressure shows. There are no centripetal pupillary fibers specially for vision (Hess). The elements which receive the light stimuli also carry those causing reflex activities in the eye. These pass by way of the chiasma to the region of the geniculate bodies to the quadrigemina. At this place a branch passes to the sphincter nucleus.

Bumke, commenting upon the observations of Bechterew, Flechsig and Edinger, states that the connecting neuron does not commence in the external geniculate but that the pupillary fibers of the optic nerve pass immediately behind the chiasma before it becomes the optic tract, *i. e.*, in the central gray matter on the floor of the third ventricle and go thence by means of a second neuron to the oculomotor nucleus. In favor of this hypothesis is the intactness of pupillary activity after uni- and bilateral interruption of the optic tract. Mention has already been made of the course of the centripetal part of the reflex from the oculomotor nucleus to the ciliary ganglion.

Karplus and Kreidl have recently added some noteworthy observations to this much discussed question. Contrary to the results of others, these experimenters, working with monkeys, were able to show that the pupillary fibers did pass into the optic tract but did not

enter the external geniculate body; they passed between the two geniculates, through the arm of the anterior corpus quadrigeminum and could be followed thence to the anterior lateral border of this body. Section of these fibers caused reflex immobility of the pupil with conservation of pupillary reactivity and accommodation, convergence and psychic activities.

If chronic meningeal or cerebral changes could be demonstrated in this locality in tabes dorsalis, we should be able to understand the Argyll-Robertson pupil.

The myosis occurring in voluntary convergence and accommodation may be regarded as a by-product due to excitation of the oculomotor. Under physiological conditions the converging reaction is much more active than the light reaction. Also the part played by the dilator is minimal.

The continuous minute oscillations or psychic reactions of the pupil are dependent upon various nervous and psychic influences as pain, fear and joy and disappear simultaneously with the light reflex in tabetics and paretics. The upper parts of the brain are not necessary for the sympathetic reflex and the pain reflex is carried via the midbrain.

The dilatation of the pupil due to psychic changes is probably dependent upon a change of tone in the oculomotor nerve having its beginning in the cerebral cortex. This is assumed since the dilatation can occur even though the cervical sympathetic be removed, but disappears if the oculomotor is paralyzed. The ordinary dilatation of the pupil is the resultant of the centrally inhibited tone of the sphincter on the one hand and of the dilator on the other. This seems automatically controlled and may be influenced by various parts of the cortex.

How may the relations of the cortex to the pupillary innervation be explained? Besides pain mydriasis, which is caused by the larger part of the cortex and is explained by cortical inhibition of the tone of the sphincter, there are two mechanisms which are carried out by means of the sympathetic and are reflex stimulations of this. Karplus and Kreidl established a subcortical sympathetic center in the medial part of the front of Luys' corpus subthalamicum. This may be activated either directly or from the frontal lobe of the cortex. This center was described as separate from the center at the base of the midbrain. Sympathetic pain mydriasis, according to this idea, is not produced in the cortex but by a reflex passing to the midbrain which acts so as to increase the tone of the dilator. Both autonomic and sympathetic activities in the brain are thus independent of each other.

The following conditions of pupillary activity are of great clinical importance and will be discussed seriatim. (1) Complete immobility. (2) Reflex immobility. (3) Dilator or sympathetic paralysis. (4) Inequality and deformity of the pupil.

1. Absolute or complete pupillary immobility. All stimuli via the vegetative nerves to the muscles of the iris are absent except a minimal effect of the sympathetic. When the sphincter is paralyzed this influence upon iris activity is next to nothing. The pupils are dilated more than normally and are somewhat distorted. Since the ciliary ganglion automatically maintains a certain amount of tone in the sphincter muscle, destruction of the ciliary ganglion or nerves causes an almost maximal dilatation greater than is observed in disease of the nucleus or root of the oculomotor. Absolute immobility is observed in syncope, central lues, epileptic attacks, occasionally in hysterical attacks, and in very marked fear. Immobility in the mydriatic state is due in these cases to inhibition of cortical origin, immobility in the myotic state to an increase of the sphincter tone (Bumke).

2. Reflex or isolated immobility is more difficult to explain. This is the Argyll-Robertson phenomenon. Its characteristics are uni- or bilaterality, failure to react to light thrown either on the same or other side, intact vision, narrowness, inequality and irregularity of the pupillary outline, retained reaction to accommodation and convergence. Excepting a very few instances of chronic alcoholism (Nonne) this condition of the pupils is diagnostic of metasyphilis, particularly tabes and tabo-paresis with involvement of the posterior columns. The question as to the genesis of this condition and particularly the myosis which so often accompanies it is of great theoretical as well as of practical importance. It has been one of the most frequently discussed questions in neurology for several decades.

The old explanation of the myosis given by Romberg still holds. He maintained that the absence of sensory stimuli due to the disease of the posterior columns was the cause of the small diameter of the pupil. The immobility is much harder to explain. The following are some of the facts concerning this condition. (*a*) The condition is often unilateral. (*b*) There is rarely absence of the convergence reaction. (*c*) Since the sensory collaterals are known to be a special locus minoris resistentiæ, it is very probable that the sensory and motor parts of the reflex arc remain intact in tabes and that the lesion is to be sought for at the nucleus of the sphincter, *i. e.*, where the centripetal influence is changed into the centrifugal, in other words at

the point where the protoneuron spreads out and breaks up into small processes which embrace the ganglion cells of the centrifugal fibers.

Since the "immobility of the knee," absent knee-jerk (Westphal's sign) has been ascribed to the degeneration of the reflex collaterals, the adjacent motor ganglion cells of the spinal gray matter remaining intact, Bumke asks, and quite justly, why this cannot be applied to the pupillary fibers and serve as an anatomical explanation of the reflex immobility of the pupil. "If one imagine such an absence of axis cylinder endings in the region of the sphincter pupillæ nucleus (and a replacing mass of glial fibers), the result must be a unilateral and isolated unreactibility of one pupil to light, and one only, the reaction to convergence as well as vision remaining intact. Naturally the anatomical basis of the sign, as the sign itself, will usually be found on both sides." In another place Bumke states that the demonstration of the absence of these fibers by a Weigert or a Marchi stain does not enter the question. There might be nothing but a mass of glial growth in place of the defect.

It is extremely doubtful whether we could differentiate by anatomical means those cases of tabes and dementia paralytica which did and those which did not have an Argyll-Robertson pupil in spite of the frequency of these metasyphilitic diseases. The way in which the Argyll-Robertson pupil might be explained in man on the basis of the animal experiments of Karplus-Kreidl has already been stated.

3. The picture of sympathetic or dilator paralysis is known in physiology as Budge's symptom complex, in the clinic as Horner's symptom complex. In addition to vasomotor and sweat anomalies, it is characterized by sinking in of the eyeball, narrowing of the lid slit (m. orbitalis), lowering of the upper lid and raising of the lower lid (m. tarsi), narrowing of the pupil (m. dilator pupillæ) and retention of the psychic and optic nerve reflexes of the pupil.

In experimental section of the sympathetic the paralysis lasts only until the preganglionic part of the sympathetic chain again joins the preganglionic and the postganglionic the postganglionic.

The contrast between the very active sphincter contraction and the equally sluggish relaxation is typical of sympathetic paralysis (Bumke).

The localizing value of a diagnosis of sympathetic paralysis or irritation is self-evident. Both conditions indicate pressure upon the sympathetic chain due to a tumor, a traumatic lesion of the spinal cord (hematomyelia), or a tumor, degenerative process (gliosis) or

an infective process in the upper dorsal segments of the spinal cord involving Budge's center. More rarely a lesion of the oblongata (thrombosis of the posterior inferior cerebellar artery, syndrome of Babinski-Nageotte) or a lesion of the spinal roots in the cervico-dorsal region (neuritis syndrome of Dejerine-Klumpke). The sympathetic lesion may be localized in its cervico-dorsal, bulbar or basal parts according to the accompanying symptoms (disturbance of the hand muscles, tongue, deglutition apparatus, trigeminus).

Pharmacological experiments with sympathicotropic substances during the last few years have added something to the differential diagnosis of sympathetic disease. For this cocain and adrenalin mydriasis have been used. These tests can be easily performed provided there is a healthy, uninjured, not inflamed conjunctival sac which is absorbing normally.

Cocain in a moderately strong solution (under 3 per cent.) stimulates the dilator. Absence of cocain mydriasis indicates weakness of the sympathetic. If a paralysis has been shown by this method in the absence of other signs, it becomes necessary to discover the location of the lesion for prognostic and therapeutic reasons. Whether it be preganglionic or postganglionic, above or below the superior cervical ganglion and whether it be in a place accessible to the surgeon. The very active endogenous hormone, adrenalin, will settle this question. A 1 per cent. solution dropped into the conjunctival sac normally produces no reaction. (2 drops are dropped in every five minutes for three times [Cords].) If the irritability of the dilator be increased as is the case in postganglionic disease dilatation of the pupil will result after fifteen minutes.

As has been stated before, it is probable that after the nerve to the dilator is gone the contractile muscle tissue becomes more irritable. (Munk's isolation phenomenon, Langendorf's paradoxical mydriasis). This adrenalin mydriasis is analogous to the rapid and maximal dilatation of the pupil after electrical, sensory or psychic stimuli in animals in whom postganglionic section of the sympathetic has been experimentally secured.

In many instances of disease involving in some way the region of the anterior or middle cranial fossæ (orbital disease, fracture of the base) adrenalin mydriasis has been observed. The explanation of this is that the sympathetic fibers going to the eye come from the carotid plexus and join the 1st branch of the trigeminal nerve distal to the Gasserian ganglion. A combination of disease of the 1st branch of the trigeminal with the adrenalin mydriasis of postganglionic sympathetic paralysis can therefore be of great localizing

value and makes an exact localization of the fracture, fissure or tumor of the base quite possible.

Bilateral mydriasis occurs as well as unilateral in diseases of internal secretion (pancreas diabetes, hyperthyroidism). This indicates an increase in the irritability of the entire sympathetic system.

A. Deformity of the pupils (asymmetry, irregularity) and inequality (anisocoria) are sometimes congenital, usually, however, acquired and of organic origin. The cause is most frequently syphilis in some form. Sometimes local disease as pressure upon the cervical sympathetic will cause the deformity. Transient inequality of the pupils is often found in severe unilateral migraine or in myalgias of the head and neck muscles with painful points in the neck (inequality due to pressure of the contracted muscle upon the cervical ganglion).

Hippus of the pupil and rapid mydriasis are of very slight clinical value.

From the point of view of vagotonia, the eye shows many signs worth clinical investigation. The vagotonic shows lacrimation and accommodation spasm which is relieved by atropin. The reaction of Löwi (positive adrenalin mydriasis) in diabetes and Graves' disease shows a lowered sympathetic tone. If there be spastic conditions in other vegetative regions as gastric crises, asthma nervosum, acute myosis will be found as an accompanying evidence of spasm. The opposite to vagotonia, *i. e.,* stimulating the sympathetic is shown in some cases of Graves' disease by paralysis of convergence (Moebius' sign) and exophthalmos (spasm of Müller's muscle).

Atropin acts slowly but persistently upon the pupil of elderly people, on the other hand rapidly but briefly in young people and vagotonics. v. Graefe's sign shows an increased tone in the autonomic levator palpebræ. It usually follows pilocarpin instillation in young vagotonics.

2. *Lacrimal Glands.*—The last organ of the orbit to be considered is this gland. Its autonomic supply comes via the sphenopalatine ganglion, its sympathetic via the superior cervical ganglion. Stimulation or paralysis of the cervical sympathetic causes respectively increase or decrease of the secretion of tears. The postcellular fibers from the cervical ganglion—secretory or vasomotor—pass upward in the inner carotid plexus and reach the gland either by the ophthalmic plexus or the cavernous plexus and the lacrimal nerve, a sensory branch of the trigeminus.

The bulbar autonomic supply corresponds to the general diagram of communicating branches given in a previous section. The af-

ferent tract comes from a motor nerve and is sheathed. This goes to a ganglion and leaves this, sheathless, to continue in connection with a sensory nerve. The white radix motorica of the sphenopalatine ganglion springs from the facial nerve and is called the major superficial petrosal nerve. The gray postganglionic fibers pass with the zygomatic and lacrimal nerves of the trigeminus to the lacrimal gland.

The bulbar centers for the lacrimal glands and the nasopharyngeal mucous membrane lie in the region of the facial nucleus. They are composed of small ganglion cells and are like the paracentral cells of the spinal cord in circumference, form and staining qualities. The sphenopalatine ganglion lies near the nasal mucous membrane. It is hard to preserve or stain. It has connections with the sympathetic. This connection is a thin bundle of fibers from the internal carotid plexus. This bundle lies in the vidian canal and is called the deep petrosal nerve. It is postcellular and sheathless.

For many animals stimulation of the conjunctiva will arouse the lacrimal glands to activity. Pain, psychic changes and emotional changes cause lacrimation in the elephant and man only. Anatomical relations explain the lacrimation occurring in superior trigeminal neuralgia and high facial palsy (unilateral weeping). The sympathetic tracts go to the periphery via the lacrimal nerve while the autonomic excitolacrimal fibers leave the facial above the geniculate ganglion and pass to the sphenopalatine ganglion.

3. *Mucous and Salivary Glands of the Head.*—Before passing on to a discussion of the vegetative innervation of the alimentary tract, we must devote some time to the mucous and salivary glands of the mouth, nose and pharynx, a group closely related to the alimentary functions. The four ganglia, sphenopalatine, otic, submaxillary and sublingual, so classically investigated by Müller and Dahl, require description at this point.

(*a*) The sphenopalatine ganglion, which has already been mentioned in conjunction with the lacrimal gland, supplies the mucous glands of the nasopharynx and the autonomic vasodilators of the mucous membrane (the vasoconstrictors are derived from the sympathetic).

(*b*) The otic ganglion receives its afferent fibers from the glossopharyngeal nerve. It is closely related to the parotid gland. The radix motorica of the ramus communicans albus of the ganglion is the N. tympanicus or more properly speaking its continuation as the minor superficial petrosal. The gray postcellular fibers leave the ganglion in the auriculotemporal branch of the trigeminus (a

sensory branch) and go to the parotid gland. There is the usual sympathetic anastomotic branch, in this case, fibers from the middle meningeal plexus.

The autonomic bulbar center has been described as Kohnstamm's nucleus salivatorius inferior, lying between the motor nucleus ambiguus and the inferior olive.

The parotid gland is also supplied by the cervical sympathetic, which sends secretory fibers or vasomotor fibers affecting secretion. It has long been known to physiologists that autonomic stimulation produces a secretion quantitatively and qualitatively different from that produced by sympathetic stimulation. Experimental section of the nerve supply and clinical observations of the absence of parotid function due to lesions of the tympanic nerve in middle ear operations have familiarized us with the function of the parotid gland tracts.

(*c, d*) The ganglia of the lower jaw salivary glands, the sub-maxillary and sublingual have almost identical anatomical and physiological relations. The first of these only will be described and Müller and Dahl will be followed. The sheathed ramus communicans albus of the submaxillary ganglion leaves the facial nerve as the chorda tympani and then joins the lingual nerve. It produces a secretory as well as a vasodilator effect upon the gland. The sheathless postcellular fibers are quite short and lie entirely in the gland, since the outlying ganglion is situated there. The autonomic bulbar center for the salivary fibers lies, according to Kohnstamm's researches, above the facial nucleus (nucleus salivatorius superior). He draws this conclusion from section of the chorda tympani and subsequent tigrolysis in the ganglion cells in the above mentioned region.

There is also a sympathetic nerve supply to the submaxillary and sublingual glands. This causes both secretion and vaso-constriction. The scanty, viscid secretion thus produced has long been known by physiologists and forms a contrast to the thin, abundant chorda secretion. It is very probable that the autonomic nerve is secretory, controlling water and salt excretion, while the sympathetic nerve is trophic, controlling the secretion of organic components.

The secretion of the salivary glands may be reflexly produced, via the sensory fibers of the trigeminus supplying the mouth, the sensory fibers of the chorda tympani or the taste fibers of the glossopharyngeal, by severe pain or psychic influences springing from various parts of the brain.

Of the better known drugs the following are of interest.

Atropin paralyzes the autonomic, adrenalin and cocain stimulate the sympathetic.

Xerostoma (Hutchison) is a little known nervous disease of the salivary glands. It is not unusual in old people (atrophic senile xerostoma) and often leads to glossodynia. It is frequently observed as an independent disease in individuals with vasomotor instability (Curschmann) and in psychopaths, related to a fear of dryness (xerophobia of actors). The neurological character of this idiopathic form is shown by its dissociation in that the lack of saliva occurs during speaking and singing, during excitement and depressing emotions, while it is absent in chewing and swallowing.

4. *Sympathetic and Vagus in the Cervical Region.*—Before leaving the vegetative end organs, we shall give a short résumé of the rôle of the sympathetic and vagus in the innervation of the head region. The autonomic innervation comes from the mesencephalic and bulbar centers.

(*a*) Sympathetic. The large shaped, superior cervical ganglion, about 2 cm. long, lies at the base of the skull. It gives off a large nerve, the internal carotid, which passes into the plexus of the same name. This ganglion has a histological structure like that of the sympathetic chain ganglia (cells with large dendrites passing through the cell capsule, more rarely with small intracapsular dendrites). It receives its preganglionic from the thoracic spinal cord segments via the cervical sympathetic. Some of the gray rami pass to the upper sensory peripheral cervical nerves. The upper cervical ganglion supplies through the internal carotid plexus the following organs:

1. M. dilator pupillæ.
2. M. Mülleri (smooth muscle).
3. Lacrimal gland.
4. Salivary glands.
5. Pilomotor muscles of the face.
6. Vasoconstrictors of the face.
7. Sweat glands of the face.

The signs of absence of function of the cervical sympathetic and its upper ganglion are well known and have been known for many years. They are due to long lasting compression or trauma.

1. Narrowing of the ipsolateral pupil, its reactivity being retained.
2. Narrowing of the ipsolateral lid slit.
3. Retraction of the eyeball (enophthalmos).
4. Hyperemia of the ipsolateral face and head area.
5. Transitory anidrosis of the ipsolateral face and head area.

The motor part of Horner's symptom complex, ptosis, miosis, enophthalmos is always present, while the vasomotor, trophic and secretory disturbances are only present in deep lesions. The accompanying symptoms are of value in a topographical diagnosis, atrophy of the tongue, vocal cord paralysis, thenar atrophic, etc. (Minor).

We have included the mucous and salivary buccal glands as a part of the digestive tract and of course the muscles and glands also form a part of it. Examples are the stomach, intestines, liver and pancreas. This part of the visceral system, as well as the mucous and salivary glands, is supplied by both nervous systems, autonomic and sympathetic. The autonomic supply of the digestive organs below the pharynx is the vagus.

(*b*) The vagus nerve, like the oculomotor, facial and glossopharyngeal, is not of pure vegetative nature, though the majority of its fibers are for glands and smooth muscle. The location of the vagus nuclei in the medulla is like that of the anterior lateral and posterior cell groups of the spinal cord. The somatomotor nucleus ambiguus lies mainly ventral and is composed of large multipolar ganglion cells, which are very similar to anterior horn cells. Their fibers go to voluntary muscles—pharynx and larynx. The nucleus solitarius lies more dorsally. It is sensory and corresponds to the posterior horn with its substantia gelatinosa Rolandi. It supplies the mucous membranes of the pharynx and larynx. The third largest nucleus lies on the floor of the fourth ventricle and is called nucleus dorsalis vagi. This is visceral and supplies the heart, lungs and gastro-intestinal tract. Its ganglion cells resemble those of the paracentral nucleus of the spinal cord (lateral column).

All the fibers which leave these three nuclei pass through the ganglion jugulare and nodosum to become the vagus. The nerve probably passes through two ganglia because it represents two nerves phylogenetically.

The ganglion nodosum resembles a spinal ganglion for it has no multipolar ganglion cells, *i. e.,* vegetative elements. Whether the ganglion jugulare, in which a few vegetative ganglion cells are to be found, represents an intervertebral ganglion like the ciliary or otic, and gives rise to post-ganglionic fibers to the viscera is hard to say, first because there are so few vegetative elements in the ganglion and secondly because there are many ganglion cells in the viscera near the entrance of the vagus fibers. The histological structure of the jugular ganglion is of theoretical interest because vegetative and spinal ganglion cells are intermingled, a developmental union of an intervertebral and a vertebral ganglion.

The fibers of the vagus in passing through the jugular ganglion certainly recall vegetative structure. That it may be a synapse is suggested by the fact that an anastomosis is made with the sympathetic superior cervical ganglion.

The next consideration is the branches of the nuclei and ganglia of the vagus.

1. Pure motor—rami pharyngei.
2. Pure sensory—ramus meningeus and laryngeus superior.
3. Mixed motor-sensory-vegetative—ramus laryngeus inf. s. recurrens (motor to larynx, sensory to trachea, visceral to the heart, aorta and laryngeal vessels).
4. Pure visceral—all other branches (for the digestive tract, heart, aorta, liver and lungs). (These will be discussed in the sections to follow.)

If one appreciates that the many centers of the medulla (for example the swallowing center) are but the places where the stimulus passes from the sensory nucleus solitarius to the motor nucleus ambiguus, the whole matter of centers becomes more readily understood, particularly the visceral centers. That there are relations of this kind has been established by section of the vagus nerve above, below and at the branching of the recurrent nerve. In the first case there is degeneration in the nucleus dorsalis and ambiguus, in the second case only in the ambiguus, while in the third case only in the dorsalis. The ganglion cells of the dorsalis are smaller than those of the other nuclei and resemble the cells in the lateral columns of the spinal cord. Visceral fibers in the vagus are recognizable by the delicate sheath.

Of the supranuclear relations of the vagus the following are noteworthy:

The motor vagus crosses the pons and the peduncles to the internal capsule and goes to the motor cortex in the region of the anterior central convolution (motor area) and the area of Broca (pharyngolaryngeal center).

The sensory vagus goes from the fasciculus solitarius and nucleus solitarius to the medial line and via the bulbothalamic tracts to the sensory cortex.

The visceral centers are not definitely known in man. In lower species they are placed in the gyrus fornicatus or supracallosus. Many authors deny the existence of these centers on a priori evidence. Jacob localizes the visceral cortex in the gyrus fornicatus or supracallosal gyri in lower animals.

5. *Gastro-Intestinal Tract.*—In passing to a discussion of the special physiology of the digestive tract, the following facts must be mentioned: The sympathetic nervous system supplies the tract from one end to the other. The vagus, besides supplying the large glands of the abdominal cavity, supplies the lower two thirds of the esophagus, the stomach, and the intestines as far as the descending colon.

Experiments with stimulation and section of nerves have given the impression that the sympathetic vertebral and paravertebral ganglia play no part in the direct control of the movements of the gastro-intestinal organs. The ganglion cells in the walls of the organs do this, while the vagus and the sympathetic fibers only exercise the regulatory functions of acceleration or inhibition.

As is well known, the vagus nerve, through its depressor nerve, has an inhibitory action upon the heart, while the sympathetic, through its accelerator nerves, has accelerator functions. In the digestive tract this is just reversed. The vagus accelerates, while the sympathetic inhibits.

Smooth muscle, unmixed with cross-striated, begins in the second third of the *esophagus*. The peripheral peristaltic waves of the gastro-intestinal tract may be inhibited through swallowing rapidly and repeatedly. In order to prove that the peripheral peristaltic waves are under control Mosso's experiment must be tried. This consists in showing that the constricting waves of peristalsis in the esophagus will proceed unhindered toward the stomach even if a circular piece of esophagus, with its ganglion cells, be cut out.

6. *Stomach.*—The stomach wall is supplied at various places by groups of ganglion cells both from the sympathetic and vagus systems. These are chiefly found in the muscularis and subserosa, but are supposed to be absent in the submucosa.

It is, of course, necessary, in order to comprehend the innervations of an organ, to understand the anatomy and histology of its nerves and ganglion cells. This applies, more than anywhere else, to the gastro-intestinal tract.

But not only in man but also in animals, there are considerable difficulties in finding out the anatomy and histology of these nerve-endings and ganglia. This is due to the fact that even in the finest specimens, impregnated with metals, the digestive juices and ferments digest the little endings of the nerves after death and after the circulation is impaired, even though the specimen be perfectly fresh and taken from a living person or experimental animal.

Among the structures of the sympathetic system, which join it as end-organs, are the nervous networks of the stomach and intes-

tines. These are the most complex in nature and have the greatest number of connections among themselves. The cells, both in size and structure, in the make-up of these fiber-networks, and in the number and type of their branches, are so varying that at this time, they cannot be classified or even described at length. This much, however, may be said, that the nerve cells from which the anatomic pictures are made up vary and are recognized and clearly distinguished according to the structure to which they belong. The various anatomic and functional localities give the ganglion cells, irrespective of their arrangement, or of their number or distribution, a cytological character, which cannot be mistaken. All cells, which are found in the digestive tract, may be divided into the two main types of cells, which have been described in the section on General Histology.

The stomach is shut off above and below by the tone of its sphincters. Above, it opens after a peristaltic wave has begun in the esophagus, provided these waves do not follow each other too rapidly. Below, it opens rhythmically, after food has been taken, provided the intestine is not full.

Consequently at one moment the sphincter pylori relaxes, at the next the cardiac sphincter does the same.

Visual, auditory and olfactory sensations have a marked psychic effect upon the gastric secretion. This varies both in quantity and quality, according to the stimulus (meat, bread, milk).

The following experiments, with bilateral vagotomy, show the effects of this operation:

(*a*) The normal influence of chemical agents (meat extract), which act either directly upon the glands or through the blood, is little changed.

(*b*) The reflex psychic secretion of gastric juice is stopped.

(*c*) There is a severe, though transitory, paralysis of the stomach musculature.

(*d*) Those inhibitions of the flow of gastric juice which follow and are characteristic of mental pain are absent.

The new experiments of Kirschner and Mangold throw some light upon the motor functions of the distal segment of the stomach after a complete cross-sectioning has been performed so as to separate the pyloric part from the influence of the vagus nerve and from that of the cardiac part.

The following functions of the stomach remain unchanged: (These observations are of great value in considering the part played by the vagus nerve in practical surgery.)

1. The tone of the sphincter pylori and the rhythm of the alternation between the closure and opening during emptying of the stomach remain normal.

2. The amount of increase in pressure due to the contraction of the antrum pylori and the rhythm and type of the contraction of the antrum remains normal.

3. The functional coördination of the sphincter and antrum pylori remains normal.

4. The chemical reflex action originating in the duodenal mucous membrane and affecting the pyloric part of the stomach remains normal.

Animals are best suited to pharmacological testing of the stomach. For this purpose either the Pawlow method—intact connections between the stomach and nervous system—should be used of the Bickel method. Isolation of the stomach from the central nervous system. In the former method, the influence of the mind is retained, in the latter it is lost. In the animals operated by Pawlow's method, atropin gradually stops the acid secretions of the stomach until the reaction becomes alkaline, while in the Bickel method this does not take place (Ehrmann).

On a former page, in discussing the sensory activities of the vegetative system, we have noted that it is not at all unlikely that the vagus carries sensations to the antrum without the assistance of any spinal tracts.

Vomiting, which is due to antiperistalsis, belongs to the realm of pathology, even though there is in all probability a bulbar center controlling it. This center is stimulated by feelings of nausea, increased intracranial pressure, cerebral concussion or intense pain (renal and liver colic). The act of vomiting is, moreover, not infrequently accompanied by manifestations of increased tone in neighboring parts of the autonomic system, as facial pallor, sweating, salivation, tachycardia and diarrhea. Centrifugal impulses pass over both the vagi and the splanchnici, not only in producing peristalsis but also antiperistalsis, yet, it is only in connection with the act of vomiting that the abdominal wall is brought into activity.

There is also a form of cerebral vomiting which is characterized by lack of any gastralgia or gagging and by the presence of headache, dizziness, somnolence and bradycardia.

The physiology of nervous dyspepsia and of vomiting in diseases of the liver and kidneys, in motor and secretory neuroses as achylia, hypersecretion or hyperacidity, in neurogenic insufficiency

of the pyloric musculature, in rumination and in diseases of endocrinous gland origin, as Graves' and Addison's diseases, is yet unsettled. Functional disturbances of the gastro-intestinal tract, as paralysis of the colon, seldom are of local diagnostic value.

The vagotonic manifestations of the stomach will be considered in connection with those of the intestinal tract.

7. *Small and Large Intestine.*—The vagus either directly or through the solar ganglion exerts a stimulating effect upon the peristalsis and secretion of the small intestine, while the splanchnic acts as an inhibitor.

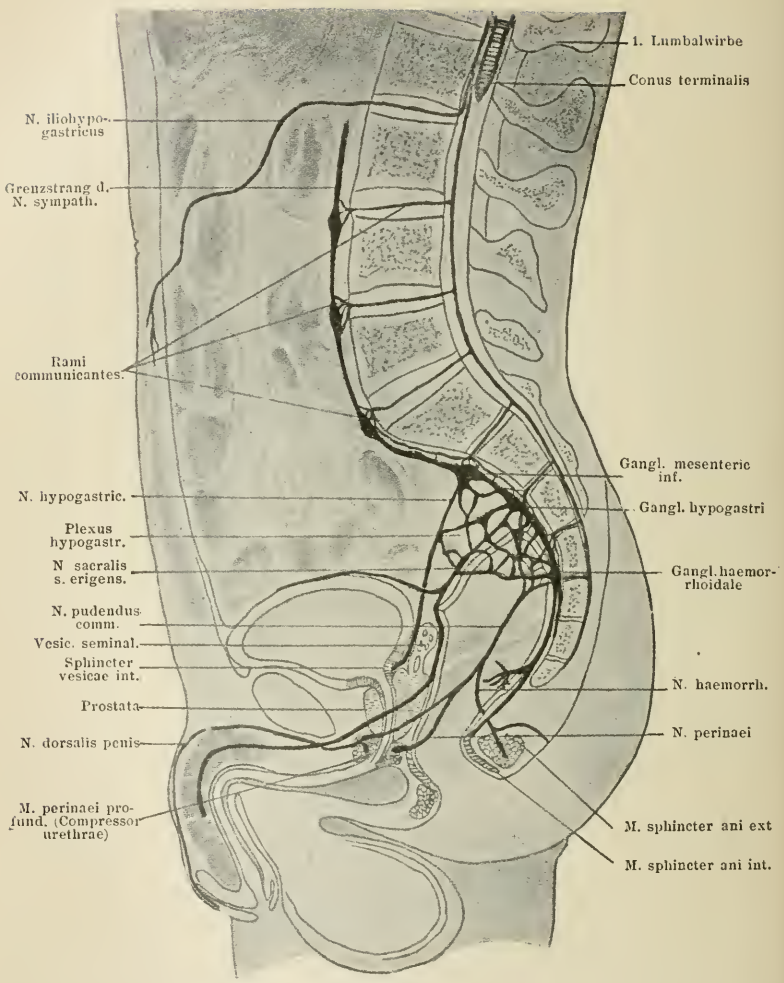
The mesenteric vagus nerves are non-medullated. The paravertebral ganglion cells contain wide dendrites and the ganglia are contained in a capsule. The splanchnic nerve in spite of its postganglionic nature contains medullated fibers.

Langley and Jacobsohn have shown that the small pear-shaped unipolar cells which give rise to the splanchnic nerves lie in the lateral columns of the spinal cord between the levels of D6 and L2.

The ganglion cells between the longitudinal and circular muscles —Auerbach's or the mesenteric plexus—seem to be sensory in nature. No fibers which could stimulate this sensory reflex arc have been shown to pass from the intestinal epithelium to these ganglia. The intestine, like the heart, has its impulse production also in its own walls. Section of the mesenteric nerves has no conspicuous influence upon intestinal peristalsis. The question of whether the stimulus to activity is myogenic or neurogenic in character has been studied by Magnus. When the longitudinal and circular intestinal muscles are pulled apart, the former, which retains Auerbach's plexus, remains normal in activity, while the nerveless circular musculature loses its automaticity, rhythmicality and refraction period of contraction.

Two groups of reflexes are supposed to take place in the intestinal tract, one tactile, mechanical, the other chemical. The first act as stimuli for peristaltic activity and continue to act even when indigestible substances are present in the gut. The chemical reflexes on the other hand have to do with changes in the tonicity of the pendulum movements. The reflex continues as long as there are any absorbable substances left in the intestine and the effect varies with the character of the substances. In gastro-intestinal disease the resorptive pendulum activities cease and only the coarse mechano-peristaltic activities remain (L. Müller).

The various types of intestinal activity (pendulum and rectopetal) depend upon rhythmic contraction of the longitudinal and



Schematic Representation of the Innervation of the Pelvic Viscera. (Braune & Müller.)

circular musculature. These may go on without the interference of the cerebrospinal axis, as experiments show, which completely isolate the intestine at the same time transecting the spinal cord and severing the vagi, thus isolating the abdominal ganglia. The intestine, is, however, regulated by the nerves passing to it (vagi, splanchnics), for stimulation of the sympathetic splanchnic causes vasoconstriction and inhibition of peristalsis, stimulation of the autonomic vagus causes vasodilatation and increase of peristalsis.

The small intestine and the ascending colon are innervated as follows:

(*a*) *Sympathetic.*—N. splanchnic superior, which passes from its nucleus in the lower dorsal cord to its peripheral ganglion, the superior mesenteric.

(*b*) *Autonomic.*—N. vagus, which passes downward into the solar plexus.

The rest of the colon, the sigmoid and rectum, are innervated as follows:

(*a*) *Sympathetic.*—N. splanchnic inferior, which passes from its nuclei as the upper lumbar segments to the peripheral ganglion, the inferior mesenteric.

(*b*) *Autonomic.*—N. pelvicus (Langley) (called N. erigens by Eckhardt), which passes from its nuclei in the lower sacral segments and comes to the pelvic ganglion in the plexus hemorrhoidalis.

The entire intestine therefore obtains two sets of antagonistic impulses:

1. Inhibition of muscular activity and blanching of the mucous membrane from the superior and inferior splanchnic nerves.

2. Increase of muscular activity and congestion of the mucous membrane from the vagus and pelvic nerves. The latter might be called the "inferior vagus."

Each of these two sets of nerves acts independently of the other. Thus the "conditioned" reflex of Pawlow or the "associative" reflex of Bechterew, *i. e.,* the psychoreflex, acts by means of the vagus upon the beginning of the digestive tract (flow of gastric juice caused by appetite, cessation of gastric activity through worry) and by means of the pelvic upon the end of the tract. There is a diminution of the tone of the terminal musculature of the digestive tract when one approaches the house in which an undisturbed evacuation can take place. "It frequently happens that after having bared the buttocks and become seated upon the toilet an evacuation takes place without any assistance from the abdominal press, while on the other hand when the attention is diverted or under the stress of business there is often no inclination to defecation" (L. Müller).

Various peripheral sensory stimuli, particularly the inhibitory effect upon intestinal activity caused by irritation of the parietal peritoneum, are entirely independent of the vagus nerve. They travel from the sensory part of the spinal cord to the motor ganglia of the intestine via the splanchnic nerves. A fact of considerable significance is that this reflex is independent of pain stimuli. Section of the vagi or of the spinal cord or ablation of the cerebrum has no effect upon the inhibitory function of sensations, while section of both splanchnics allows quiet intestinal activity to go on without any noticeable influence of pain sensations.

Section of the splanchnics or extirpation of their prevertebral ganglia not only causes increased peristalsis but also marked hyperemia of all abdominal organs, which is accompanied by outpouring of serous fluid into the lumen of the intestine. Emotional diarrhea is due to a paralysis of the splanchnics. Yet many authors maintain that this and psychic vomiting are parallel activities, one being due to increased activity of the pelvic, the other to increased activity in the vagus nerve.

The abdominal blood vessels, as least those that have a vasomotor control, behave in opposite fashion to the blood vessels of the periphery. This allows them to play a conspicuous part in the distribution of the blood in the body.

So much for the innervation of the intestine. The review shows that it is an automatically acting organ, the most important part in its activity being played by the ganglia lying in the wall of the organ, a condition similar to that of the relations of the ciliary ganglion and pupils. Every exteroceptive sensation, every psychic activity, every emotion, every change in the distribution of blood causes the ganglia to initiate changes in the intestinal activity and in the tone of the intestinal blood vessels.

The need for the coördination of the abdominal blood supply and that of the rest of the body, and of rapid changes in blood distribution in response to the nervous control of temperature is quite apparent, an observation which L. Müller has justly emphasized. At least the means by which fear and anticipation influence the activities of the intestines can be appreciated.

Returning to the consideration of separate parts of the intestine, peristalsis in the small intestine is started not only by the presence of food in the stomach, but also by the mere swallowing of food and even when the food reaches the mouth (Cash). At the very beginning of eating "psychic" secretion and motility begin in the stomach —demonstrable by sham feeding in esophagectomized dogs—and at

the beginning of gastric digestion, bile and pancreatic juice are secreted and intestinal tone is diminished. The activation of movements of the large intestine by activity of the small is readily demonstrated in animals with small intestine fistulas. Cathartics affect the small intestine but do not reach the large intestine for they are excreted through the fistula. Yet the large intestine becomes active.

In diseases of the colon, antiperistaltic activity (Böhm) is increased (x-ray examination). The antiperistalsis and peristalsis cause considerable mixing and thus water absorption. As a result the feces become quite dry and compact (constipation with chronic colitis).

The consideration of the lower intestinal tract, not innervated by the vagus, will be taken up in connection with the bladder and external genitalia, which with this part of the intestines are all supplied by the pelvic nerve.

For a discussion of the effect of intense pain (crises), drugs or hormones upon gastro-intestinal activity, the reader is referred to the general considerations. This much, however, may be recapitulated. Adrenalin causes inhibition of intestinal activity by way of the splanchnics, physostygmin and pilocarpin cause increase of intestinal activity by way of the vagus, nicotin breaks impulses at the synapses in the large prevertebral ganglia. Of the hormones, hormonal or the peristaltic hormone deserves mention. It is possibly similar to gastrin or the gastrosecretion of the English and to the other internal secretory products of the intestinal tract, proteolytic ferments and enterokinase. It was used therapeutically by Zuelzer. Some of the endocrinous glands produce substances, as for example the thyroid product, thyreo-iodoglobulin, which affect the intestine. Of late years it has been shown that the gastric mucous membrane at the height of its digestive activity produces a substance which injected subcutaneously or intravenously initiates intestinal activity. It is spoken of as the peristaltic hormone. Zuelzer's opinion of its action is that it stimulates the abdominal ganglia specifically and that thus peristalsis is begun. This peristalsis differs from physostygmin peristalsis in that the latter is lasting, not stopping with the individual peristaltic movements, while the former, the hormonal peristalsis, is like natural physiological peristalsis. If this be excessive, it stimulates the secretory glands of the intestine and thus produces a movement after meals. Popielski does not credit the hormonal theory. The extracts of all organs, not alone the stomach, contain a substance, vasodilatin, which intravenously injected causes two main phenomena, (1) diminution

of the coagulability of the blood, (2) dilatation of the abdominal blood vessels with drop of blood pressure. Popielski claims that Zuelzer's results with hormonal are due to its content of vasodilatin, and that the increase of peristalsis is secondary to autonomic drop of blood pressure and is not specific. A similar nucleoalbumin, "hypotensin," has been described (Abelous and Bardier). They isolated it from several excretions and secretions. Its main property is the lowering of blood pressure.

Secretin, which has been mentioned, is probably a product of the "chief" cells and also stimulates the motor and sensory activity of the stomach, causes digestion, leucocytosis and through venous paths, vasodilatation and a drop of blood pressure.

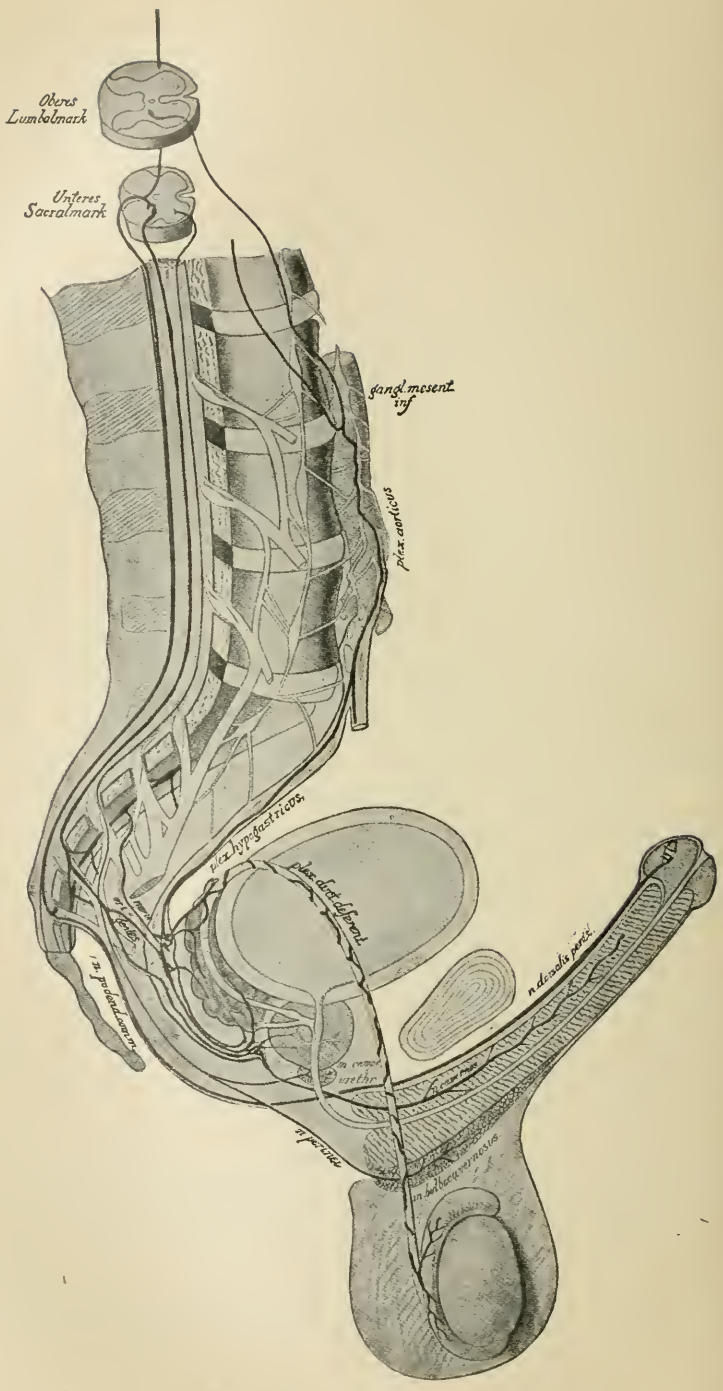
8. *Recto-urogenital Tract.*—The diagram of Meyer and Gottlieb and the older one of Müller will be followed. This demands a discussion of the excretory organs, descending colon, sigmoid and rectum, bladder and genitalia, which will deal generally with these organs and first particularly with the descending colon, etc., since this would naturally follow the discussion of the gastro-intestinal tract just preceding.

The pelvic organs are not only supplied by sympathetic hypogastric nerves and the autonomic pelvic nerve, but also by those of the cerebrospinal group. If one starts with the first sacral vertebra, where the metamere relations of the intervetebral ganglia are scarcely discernible, one finds running caudalward three large sympathetic ganglia, the superior mesenteric, the hypogastric and the hemorrhoidal. The white rami communicantes all connect with the spinal cord. The gray rami supply the uropoetic, genital and rectal organs. The comparative relations of the vegetative and somatic tracts will be clarified by the following:

1. The former, as a rule non-medullated fibers, supply smooth muscle and mucous membranes. (The hypogastric supplies the longitudinal and circular muscles of the descending colon and bladder including the internal rectal and bladder sphincters, the cavernous plexus and the N. erigens supplies the genital vasomotor nerves.)

2. The latter, as a rule medullated fibers, supply the cross-striated muscle and skin of the region with branches which are carried by the spinal N. pudendus communis (M. sphincter internus recti, M. sphincter internus vesical or compressor urethrae, MM. peronei profundi).

Vital staining with methylene blue shows multipolar sympathetic ganglion cells in all the vegetative organs mentioned in this section.



Scheme of the Vegetative Innervation of the Male Genito-urinary System.
(Miller & Dahl.)

However, the significance of the mesenteric, hypogastric and coccygeal plexi is by no means understood. The production of involuntary movements, quite independent of the voluntary movements of contraction and relaxation of the openers and closers of the organs concerned, may be mainly due to the ganglion cells lying in the wall of the organs.

Most of the reflexes in this region can be produced without the intervention of the central nervous system. There is a noteworthy difference, however, between the energetic reflex contractions of a cross-striated muscle and the slow contraction of smooth muscle.

TABLE OF REFLEXES

Reflex	Stimulus	Result
Scrotum	Repeated stroking or application of cold to the perineum.	Contraction of the tunica dartos.
Bladder	Stretching or stimulation of the bladder or posterior urethra.	Contraction of the bladder wall.
Rectum	Stretching or stimulation of the upper rectum.	Contraction of the rectum.
Genital	Psychic or peripheral stimulation.	Erection and hyperemia of the corpus cavernosum.
Uterus	Stretching or stimulation of the uterus.	Contraction of the uterus.
Internal anal	Stretching the anus with the finger.	Contraction of the sphincter.

9. *Rectum.*—The rectum is supplied by the hemorrhoidal plexus and the inferior mesenteric nerves. Centripetal fibers pass from the plexus to the spinal cord which bring to consciousness the degree of fulness of the rectum and the feeling of need of defecation. The mucous membrane of the rectum is neither sensitive to increase or decrease of weight of contents or to cold or heat, but does register the degree of stretching, so that there is an impulse to defecation as soon as the fecal mass in the sigmoid begins to be pushed into the rectal ampulla. Voluntary striated muscles do play a large part in defecation for they both begin and end it, leaving the reflex part of the act to the vegetative nervous system. The fecal mass is pushed outward with the help of the abdominal press (NN. hypogastrici). The sensory stimulation of the rectum thus produced brings about peristaltic contraction of the rectal musculature and relaxation of the sphincter internus, following which the feces are expelled from the body. Following this the voluntary muscles, levator ani and sphincter externi ani raise and close the anus.

In transverse lesions in the cervical or dorsal regions, there is absence of the activity of the abdominal muscles. If the lesion be

in the lower part of the cord, the sphincters alone are inactive. There is this big difference between lesions of the upper and lower cord regions in that, though defecation becomes regulated a while after the lesion occurs (automatism of sphincter internus), it is only in the sacral lesions that the nucleus of the sphincter externus is affected. As a result the external configuration of the anus is changed, the anus is wider, no longer radiate, closure is not so firm and insertion of the finger or stimulation of the adjoining skin does not call forth a strong sphincter contraction (anal reflex). According to L. Müller the anal reflex is the only certain diagnostic point in intestinal diseases which will localize the spinal cord lesion, for the simple reason that presence *rules out* disease of the lower sacral and coccygeal segments. Other disturbances of intestinal activity are as a rule independent of the localization and type of the spinal disease. The usual sequence is first retention, then incontinence.

The tone of the internal sphincter, as that of all other sphincters, may increase due to the activity of the ganglia in its wall after section of the nerves passing to it. After a short period the intestinal tract is again closed. Opening of the intestinal tract by inhibition of the tone of the sphincter may take place even after the spinal cord and its sympathetic nerves are destroyed.

The spinal center for defecation in the dog lies in the lumbosacral area, the cortical, posterior to the gyrus sygmoideus. In man Bechterew puts the cortical center between the arm and leg centers and the subcortical in the corpus striatum and optic thalamus near the centers for erection, ejaculation and uterine activities. The denial by Müller, Dahl and others of the existence of cortical vegetative centers has already been discussed.

The neurological disturbances in diseases of the spinal cord are typical, constipation when the stool is formed, incontinence when it is soft. The reason for this is that the feeling of fulness of the ampulla recti is not brought to consciousness due to the interruption of nerve fibers and thus the impulse to defecation does not pass downward from the brain. There results therefore a lengthy retention until the *vis a tergo* causes an involuntary expulsion of the hard fecal masses (incontinence).

According to the same author the principle which claims a defecation center in the lower part of the spinal cord is false and is so on the basis of the above mentioned data. He claims that there are only ganglion cells for the control of the external voluntary sphincter in this locality.

Finally a few other conditions deserve mention, (1) congenital motor insufficiency of the rectum, (2) hyperirritability of the rectum (peristaltic waves in tenesmus) and (3) reflex constipation.

Severe constipation and acute cessation of intestinal activity occur in conditions of intense, lasting pain. The splanchnic leads to lasting inhibition of intestinal activity in gall stone colic, renal colic, circumscribed peritonitis, contusions of the abdomen, obstructed hemorrhoidal nodules, etc.

Eppinger and Hess state that many vagotonic conditions of the digestive tract have been described. In all of these pilocarpin and physostygmin are supposed to aggravate, adrenalin and atropin in large doses to alleviate.

In the vagotonic the following conditions may be seen: salivation and increased nasal and lacrimal secretion, permanent and periodic increase in the tone of the esophageal musculature taking the clinical form of esophago- or cardiospasm. Radiographically a retarded passage through the alimentary canal may be found, due in part to increased tone of the muscles, in part to diminished peristalsis. Not only the influence of the vagus upon the salivary glands and the esophageal musculature but also its influence upon the tone, peristalsis and secretions of the gastro-intestinal tract and its large accessory glands, the pancreas and liver, is noticeable in the vagotonic. The vagotonic stomach shows by its form the increase of muscular tone. The meal is slowly forced from the fundus thorugh a narrow slowly unfolding canal. This is known radiographically as Holzknecht's cow-horn type or the spastic hourglass type. Accompanying this are powerful peristaltic waves which are indicative of the presence of all of the hyperkinetic forms of motor gastric neuroses.

Further symptoms of vagus stimulation are hypersecretion and hyperactivity. These present themselves in various ways, intermittent gastrosuccorrhea, hypersecretion with or without hyperacidity. These are sometimes associated with sphincter spasm, pylorospasm and subsequent antiperistalsis. The beneficial effect of atropin and the detrimental effect of pilocarpin are said to differentiate between pylorospasm and pyloric stenosis in the absence of any signs of motor insufficiency. The accompanying pains are radiating in type, their paths being to the vegetative centers and thence to the segmentally corresponding sensory nerves (Head's hyperalgesic areas).

The diarrhea in vagotonia (diarrhœa nervosa) in Graves' and Addison's diseases have been claimed to be due to a state of hyper-

irritability of the vagus supply to the intestine, *i. e.*, to an increase of peristalsis and an increased serous transudation into its lumen. The beneficial effect of atropin subcutaneously and adrenalin enemata seems to confirm this.

The secretory neuroses have recently been included in the same group, enteritis membranacea (Nothnagel) or mucous colitis and eosinophilic rectal catarrh (Neubauer). In this latter there are a great many eosinophiles in both the blood and the intestinal secretions.

Closely related to cardiospasm and pylorospasm are spastic constipation and spasm of the rectal sphincters, both little understood conditions as far as pathogenesis is concerned.

In severe vagotonia there occasionally occur conditions of intense spasm in the smooth muscle of the gall bladder, gall duct, ureter and bladder. Spasm of the gall bladder is said to cause spasm of the gall duct and thus by a transitory shutting off of the gall passages causes (nervous spasmodic jaundice) acholic stools, jaundice and bradycardia. The same kind of mechanism is present in reflex anuria, which may be due to spasm of the renal blood vessels.

Of the general disorders which occur in vagotonics, a few deserve passing mention. In the sphere of blood chemistry, eosinophilia; in the sphere of metabolism, high sugar tolerance and absence of adrenalin glycosuria.

10. *Bladder.*—The same conditions which hold in emptying the rectum of feces exist in the process of emptying the bladder. This organ is supplied by the nerves from the lumbar sympathetic, and the sacral autonomic. Very long rami communicantes go from the fourth lower lumbar nerves to the sympathetic cord, and from this to the inferior mesenteric ganglion. Here they are intercepted by a ganglion cell and proceed as post-ganglionic gray fibers in the hypogastric nerves to the musculature of the bladder, particularly to the internal sphincter (Tables VIII and XI).

From the sacral roots springs the sacral vesical nerve, the so-called N. erigens of Eckhardt, which, as a white ramus communicans, is interrupted in the ganglia of the hypogastric plexus, to proceed thence as the gray post-cellular branches to the detrusor muscle of the bladder.

The same conditions are therefore found here, as are found in all of the vegetative organs. For example, the pupil, which has been previously considered, also has a sympathetic dilator muscle, and an autonomic sphincter muscle.

In the conus medullaris the small pear-shaped sympathetic gan-

glion cells occupy almost the entire anterior and lateral parts of the gray matter—a blending of the inferior lateral and the medial inferior sympathetic nuclei. The bladder also has a group of ganglion cells in its musculature at the point where the ureters enter.

The mechanism of urination is like that of defecation and is arrested by the assistance of voluntary muscles. If there is a dull feeling of a full bladder behind the symphysis, the assistance of the pressure of the abdominal wall, and of an increase in abdominal pressure serves to accelerate the emptying. The spinal reflex is released; the tonus of the detrusor increases, that of the internal sphincter decreases, and thus there results, without further voluntary impulse, an emptying of the bladder with a good stream. Finally the repeated contractions of the voluntary perineal muscles about the posterior part of the urethra force out any residual urine and the sphincters are thus able to regain the usual tone which they possess when closed.

It is noteworthy that after removal of the lower part of the cord up to the middle of the lumbar region, emptying of the bladder and rectum, after an initial disturbance of the functions of these organs, becomes quite automatic and uncontrollable by the will.

According to Müller, it is questionable whether disturbances in bladder functions may lead to diagnostic conclusions as to the locality of the trouble. Frankl-Hochwart and Zuckerkandl are less pessimistic in this regard, and believe in a spinal etiology whenever the voluntary increase of pressure on the bladder is lost, and there exists at the same time automatic emptying, paralytic dribbling, expressibility, and bladder hypertrophy. They say: "Early appearance of dribbling and of expressibility may with certainty be ascribed to a disease of the cauda and conus, while a spastic condition in the sphincter, or hypertrophy of the detrusor points to a lesion higher up."

The nature of cortical bladder disturbances consists in an inability to repress the tone of the sphincter, and appears clinically in cystospasm, pollakiuria, oliguria, more rarely in incontinence and retention [Frankl-Hochwart, Zuckerkandl, Czyhlarz, Marburg, Minkowski, Hamburger]. The diagnosis of cortical bladder disturbance becomes uncertain as soon as the patient ceases to be conscious, intelligent or ceases to have the normal autoptic control of the spinal cord. Bladder disturbances have always been obtained in experimental lesions of the mid-brain, involving the gray matter near the floor of the third ventricle (Lichtenstern).

In regard to the antagonistic relations which the bladder centers

have to each other, the majority of physiologists, and recently also Lewandowsky, on the basis of his own experiments, conclude that the normal impulses to the bladder, both for closure and opening, are always initiated from the cerebrospinal axis, spontaneously or reflexly, while the integrity of the ganglia has no influence upon function. On the other hand Müller, who formerly placed the center for the control of the functions of the bladder in the sympathetic ganglion groups lying in the pelvis, is of the opinion that there is no single vesical center in the spinal cord, which influences the sympathetic. Since, in man, higher transectional disease of the cord as well as lesions of the conus cause bladder disturbances, and, furthermore, since in animal experiments both transection of the cord, and removal of the lower part of the cord result in the same type of bladder emptying, it may be concluded that localization of vesical centers in the conus medullaris is not justifiable.

11. *Sexual Organs.*—In considering the special nervous relations of the sexual apparatus, it is to be noted that the nerve plexi in the internal genitalia are derived on the one hand from nerves coming from the lumbar cord, through the lumbar rami communicantes which proceed by way of the hypogastric nerves, and on the other hand from the sacral cord and sacral roots by way of the N. erigens. Stimulation of the sympathetic lumbar rami communicantes causes vasoconstriction and contraction of the small muscle of the vas deferens and the seminal vesicles, while stimulation of the autonomic sacral rami causes vasodilatation and erection.

Erection and ejaculation have obviously separate spinal centers, the center for erection lying in the lower sacral cord, that for ejaculation in the upper lumbar cord. There are no special cortical centers for these acts.

In the sexual act the following phases are with justice sharply differentiated: the desire, erection, ejaculation and orgasm (Frübringer, Müller).

1. The concrete sexual desire appears at the age of puberty, possibly dependent upon the appearance of certain internal secretions (hormones) derived from the sex glands. It disappears immediately upon the emptying of the semen. It remains intact after section of the cord. In women it is increased after menstruation. In diseases of the cord it disappears gradually after impotence sets in, particularly when the disease has begun early, before the local sexual impulses have been normally impressed.

What substances may be libidogenous has not been finally settled upon. Most probably they are derived from the sex glands, which

at puberty produce an external secretion (sperm) from their parenchyma as well as an internal secretion from the interstitial cells of Leydig. Both secretions are in a certain sense independent of each other. Contrary to the conditions in other endocrinous organs, the internal secretion of libidogenous substances seems to be shared by the prostate and seminal vesicles as well as by the sex glands themselves.

In cases in which the libidogenous, aphrodisiac substances are lacking, as in children and eunuchs, even the most hilarious and passionate feelings, founded upon associations, are unable to bring about the sexual passion. "Our cortex, and thus our thoughts, are made more sensitive to sensuous impressions and erotic conceptions by these substances. The cortex, on the basis of association, is only able to react with a sexually active feeling when these internal secretions are present" (Müller-Dahl).

2. Erection may be considered as being brought about in three ways.

(*a*) A cerebral or psychic stimulus is the most frequent manner of arousing this vasodilator phenomenon, *i. e.,* by means of sensuous impressions, memories and conceptions. The cerebrospinal fibers leave the cord in its upper lumbar part and go thence via the N. erigens to the erectile organs. This origin is the reason for the intactness of psychic erection in lower-lying diseases of the cord.

(*b*) In the periphero-spinal reflex the N. erigens also is the centrifugal path, the centripetal being from a reflexogenic area of the skin or mucous membrane of the periphery, through the N. dorsalis penis and the N. pudendus communis, via the corresponding vegetative ganglia to the second sacral segment.

(*c*) The last way in which erection occurs, one which is automatic, is neither from the cortex nor the cord, but is due to fulness of the seminal vesicles or bladder. The nervous organ which transmits this reflex is possibly contained in some of the ganglion cells in the hypogastric plexus. If the spinal cord connections be severed this automatic reflex erection remains, but the peripheral skin sensibility is lacking and thus the individual can only be aware of the erection by inspection.

Permanent erection (priapism) in acute transverse lesions of the cervical and thoracic cord is probably due to disturbed vasomotor centers in the cord. Whether there be a form of erection not due to stimuli coming through the nervi erigentes, but due to a decrease in the tone of the vasoconstrictor fibers in the N. dorsalis penis must remain an open question (Eckhardt, Lovén, Müller).

3. In the act of ejaculation, as in all motor activities, both the sympathetic and spinal systems are to be considered.

The reflex functions of the former come into play in that the summation of adequate stimuli (rubbing movement) acting upon the erected organ causes peristaltic contraction of the smooth muscles of the three secretion-bearing organs, the vas deferens, seminal vesicles and prostate. This causes the orgasm and empties the mixed secretions into the prostatic urethra. A secondary reflex of a somatic nature now occurs, namely a contraction of a spinal cord origin of the cross striated bulbo cavernosi and ischiocavernosi muscles which act forces the semen out of the prostatic urethra.

The vegetative arc of this reflex mechanism is seldom disturbed, while on the other hand the somatic arc frequently is injured by spinal cord lesions, particularly deep-seated diseases of the conus. When this injury occurs there is also disturbance of the mobility and sensation of parts supplied by near-by muscles. The semen under these latter circumstances is not forcibly ejaculated, but flows off drop by drop.

The relaxation following ejaculation is partly due to a passive process, decrease in tone in the NN. erigentes, partly to an active process, contraction of the smooth muscle of the skin of the penis and of the erectile bodies. Nocturnal flow of semen during sleep or pollution may occur without sensory stimuli acting upon the individual and may yet be accompanied by the marked and well-known feelings of passion. This may be called orgasm and is regularly accompanied by the manifestations of stimulation in the rest of the vegetative system (mydriasis, hyperidrosis, and tachycardia).

The antagonistic innervation of the genitalia is seen in the fact that when the tonus in the lumbar sympathetic part of the cord decreases, that in the sacral autonomic part increases (Langley).

Among the vagotonic symptoms in the pelvic region are the following: Tenesmus, dribbling, erection, spermatorrhea, and prostatorrhea. The sympathetic disturbances in the female genitalia are atony of the uterine muscles with atonic or so-called genuine hemorrhages, more rarely inversion of the uterus.

It must be said of the uterus that its contractions are automatic. Thus there are cases of painless though normal births, with subsequent uterine contractions, even when disturbances exist in the lower part of the cord.

That psychic stimuli and sudden pain have great influence upon all the ano-vesico-genital reflexes is well known. Incontinence of feces during fear, involuntary micturition during terror, cessation of

labor pains during grief, decrease of libido and the power of erection during strong emotional strains, nausea, and when feeling of satiation exists, show this to be so.

12. *Respiratory Tract.*—Little of a positive nature is known about the respiratory tract. It is claimed that fibers pass from the sympathetic cord to the bronchi which relax the bronchial musculature and which also dilate the bronchioles and increase the lung capacity in the deepest branches of the bronchi. Groups of multipolar ganglion cells are to be found. These are of a viscero-motor nature and in structure like those in the sympathetic cord. Ganglion cells of the spinal ganglion type with one or more dendrites are also to be found in the bronchi where the bronchial plexus is formed by the vagus. These are in all probability viscero-sensory in nature (Müller).

The superior laryngeal nerves, the brachial and the bronchial nerves—all autonomic vagus fibers—carry sensations from the mucous membranes, which they supply, to the domain of consciousness, and upon stimulation cause inhibition in the respiratory center in the form of a cough-reflex, as in inflammations, accumulations of mucus, pressure of foreign bodies, poisonous gas, and dusty air. It appears that these fibers are solely sensory in nature and not vegetative.

The smooth muscle of the bronchi is supplied by the motor visceral vagus. Stimulation of this nerve does not give relaxation but always contraction. In bilateral section of the vagus, the bronchi are dilated, and breathing is slow and deep, while stimulation of the vagus causes inhibition of inspiration followed by expiratory cessation of respiration.

Clinically, acute bronchio-spasm or asthma must be considered. This is characterized by lack of breath, marked difficulty of expiration, slowing of the respiratory phases, blanching of the lungs and viscous sputum filled with eosinophils. In paroxysmal increase of the tone of the vagus, spasm and hypersecretion is not only seen in the bronchial muscles, but also in the laryngeal muscles (laryngospasm) and is associated with nervous symptoms in other branches of the vagus. The reflexogenic zones lie in the bronchi, nose and many other parts of the body. Emotional excitement as anger, or sexual emotion may, as observed above, favor and cause these attacks.

In the realm of pathology further mention must be made of the laryngeal crises of tabetics, the respiratory arrhythmias of vagotonics (cessation of breathing, arrhythmia or pulsus irregularis respira-

torius infanto-juvenalis), narrowing of the glottis or the laryngospasm of tetany, and stoppage of respiratory movements after pressure upon the eyeball, all of which manifestations, on the one hand, are increased by pilocarpin, and on the other are somewhat diminished by atropin.

Of these manifestations, those lending themselves readily to mechano-physical investigation, as respiratory arrhythmias and Aschner's respiratory standstill, are particularly to be noted.

Pulsus irregularis respiratorius, as is well known, consists in an acceleration of the heart beat and a decrease in the pulse volume during inspiration, while expiration makes the pulse fuller and slower. According to Hering, this phenomenon is particularly frequent in young persons, and is to be identified with Mackenzie's "infantile type" of respiratory arrhythmia. This arrhythmia presupposes the presence of an increased tone in the inhibitory vagus fibers to the heart. It can only be considered pathological when it occurs during gentle breathing.

Aschner's phenomenon of pressure upon the eyeball has been less studied. It may be elicited in vagotonic persons by pressure upon the eyeball, or after stimulation of any of the branches of the trigeminus. The results are expiratory standstill, or at least bradycardia—the decrease being as much as to 10 beats per minute.

According to Miloslavich, this reflex is always present in epilepsy, never in hysteria.

13. *The Heart.*—The heart receives many different kinds of nerves from the sympathetic and vagus, in spite of the fact that it is an automatically acting organ.

These nerves, receiving impulses from the cerebrospinal axis, have antagonistic actions upon the heart beat, some accelerating, some inhibiting it.

Histologically there are:

1. Vagus nerve fibers to the heart, of which the majority are unsheathed.

2. The extracardiac ganglion of Wrisberg, lying between the pulmonary artery and the arch of the aorta. This may be designated as a vertebral ganglion of the sympathetic cord. It is about the size of the head of a pin, and has large round or oval cells which give branches in all directions.

3. Many intracardiac groups of ganglia which, with encapsulated ganglion cells, resemble the head ganglia.

The accelerating sympathetic fibers are supposed to be connected with the extracardiac ganglia, the inhibiting vagus fibers with the intracardiac ganglia (Hering, Aschoff).

The sympathetic tracts to the heart arise from the first to the fifth dorsal segments, are interrupted in Wrisberg's ganglion, and proceed as post-articular fibers without further interpolation of ganglion cells to the musculature of the ventricles of the heart. They have no influence upon the complicated conduction system of the heart. It is not thus with the vagus supply, which is triple. One branch springs from the superior laryngeal nerve, one from the recurrent laryngeal nerve, and the third from the thoracic part of the vagus. The branches which proceed from the heart to the aorta are mainly depressors. The right vagus supplies the deeper layers of the heart, the left goes to the superficial cardiac plexus, whereby its branches lie mainly between the arch of the aorta and the pulmonary artery near the ganglion of Wrisberg. Small ganglion cells are found at all the end branches of the vagus.

When it was first discovered, that besides the ordinary auricular and ventricular musculature there exists a special conductive system, uninfluenced by the former, namely the bundle of His, and the bundle of Hill and Mackenzie, and further, when it was discovered that there exist muscular nodes or ramifications from these bundles, as the node of Aschoff and Tawara at the entrance of the coronary veins, and Keith's node, at the sinus of the venæ cavæ, it was thought that these discoveries would bring the myogenic theory to a final victory, particularly since the fact of resuscitation of the excised heart for days could readily be correlated with the above mentioned discoveries.

The balance of opinion, however, is again swinging to the old neurogenic theory, which is favored by the presence of large numbers of ganglion cells in the heart musculature. The intracardiac ganglion cells, whose function according to many physiologists and clinicians is viscero-motor, are most thickly distributed just where the muscular conduction system begins:

1. At the place of origin of the auriculo-ventricular bundle of His and at Tawara's node.

2. At the orifices of the superior vena cava in the right auricle, where the embryonic muscle node, called the sinus node, or node of Keith and Flack forms the beginning of the cavo-auricular bundle.

In order to make certain the question of the autonomy of the heart, Lyon tried the following experiment on dogs: When the carotid and vertebral arteries are tied off, the heart after a brief time comes to a standstill. If the brain be perfused with blood the heart will beat again. Thus merely restoring the function of the brain suffices to recommence the vanished automatism of the heart.

Thus, the cerebral nerve organ may itself call forth heart beats. This observation is as difficult to reconcile with a myogenic origin of the cardiac autonomy as are the groups of ganglion cells piled up in those muscle nodes which are the site of the origin of the nervous impulse which regulates heart action.

In favor of the viscero-motor nature of these ganglia, Müller cites much physiological data, as Stannius' experiment, as well as pathological conditions, such as Adams-Stokes Disease, and anatomical peculiarities, such as the piling up of ganglion cells on the end branches of the motor vagus fibers.

The vagus tracts seem to act upon the muscle through the intervention of ganglion cells, in that the activity of the ganglion cells is inhibited, but not arrested, by these tracts.

Whether the sympathetic spinal center of the heart may be reflexly influenced, as is the cardio-respiratory center in the medulla, cannot be as definitely stated. The classical "klopfversuch" of Goltz causes in frogs stimulation of the medulla, with cessation of the heart beat in diastole.

The types of irregular pulse of vago-sympathetic origin, as well as the positive and negative influences of the cardiac nerves, have already been discussed in the section on physiology.

It is quite difficult to explain the manifestations of sensory stimulation in heart disease if one regards all the sympathetic ganglion cells as viscero-motor. It has been supposed on the one hand that there are viscero-sensory fibers in the depressor nerve of the vagus, and that on the other hand the cardiac manifestations due to fear are caused by vaso-motor disturbances of the caliber of the coronary vessels. The uncomfortable feelings of those with heart disease are probably transmitted through the sympathetic rami communicantes, via the spinal ganglia, or directly to the spinal cord, and thus are carried to consciousness, the hyperalgesia and brachial pains of Head being explained as a radiation up and down the spinal cord. The vagus has no anatomical relation to these latter phenomena since vagus fibers are nowhere in near relation to fibers going to the arm.

If one denies the existence of vegetative centers in the cortex as well as the existence of a brain center for the actions of the heart and lungs, one must regard the gray matter of the midbrain in the vicinity of the floor of the third ventricle, or, in other words, the bulbar-autonomic dorsal vagus nucleus, as the real end station. The tonus of this station is affected by affects, bodily pains and local stimuli, with resulting palpation, cessation of cardiac action and arrhythmia.

Among local stimuli must be mentioned that passing through the depressor nerve of the vagus, when the pressure in the aorta rises. This stimulation results in a slowing of the heart.

The antagonistic action of many drugs upon the heart has already been noted. Adrenalin, by stimulating the sympathetic accelerator nerve, causes an increase in the force and weight of the heart beat, while atropin, by paralyzing the depressor nerve of the vagus, also causes an increase in the rate of the heart beat.

As signs of local vagotonia in the domain of the heart, we have enormously stimulated or depressed heart activity in young people, which after atropin either disappears or is transformed into a tachycardia.

Not infrequently phrenodynia is noted, with the uncomfortable feelings of momentary cardiac standstill, and of sudden flow of blood to the head. Great lability of the heart action with variations in the pulse frequency up to an arrythmia is also found.

Bradycardia is noted in convalescence from quite a few infections as well as in conditions having a rise in intracranial pressure, in digitalis therapy, and in certain kinds of goiter hearts.

If in vagotonic bradycardias the vagus stimulus between auricle and ventricle is disturbed, a discontinuance of conduction is obtained, the auricle beats more frequently than the ventricle, and a "nervous heart block" results. This may be relieved by atropine with the result that the loss of ventricular systoles is eliminated and the rhythm is restored to normal. Should the disturbance be organic, this will not be the case.

Many forms of angina pectoris seem to depend upon stimulation in the autonomic nervous system. Stimulation of the vagus can undoubtedly cause a spasm in the muscles of the coronary arteries, and so a narrowing of the cardiac vessels. Drugs which paralyze the vagus and dilate blood vessels exert a beneficial influence upon vasomotor angina cordis. Langendorff concludes, from his experiments with suprarenin, that the sympathetic supplies vasoconstrictors to the lungs and vasodilators to the blood vessels of the heart.

Stimulation of the mucous membrane of the nose, pressure upon the eyeball (Aschner's phenomenon) and faradic stimulation of the peripheral endings of the trigeminus will influence the vagus via the trigeminus, causing a bradycardia (Eppinger and Hess). Intravenous injections of adrenalin cause cardiac irregularity only in vagotonic individuals.

In addition to vasomotor angina pectoris, disturbances in the

vago-sympathetic system are found. These manifest themselves as paroxysmal tachycardia, or bradycardia, allorhythmia or cardiac irregularity, fluttering and irregularity of the individual contractions, or irregularity of the pulse; all of these may be noted, particularly, in hystero-neurasthenic individuals.

It is worth mentioning the following conditions of irregular pulse, observed by means of the sphygmograph: pulsus irregularis perpetuus, irregularis alternans, irregularis respiratorius, irregularis extra systolicus and disturbances in the conduction of the stimulus. In the two latter, the trouble may start in the auricles, ventricles and bundles of His. The recently described asphygmatic pulsus alternans, or asphymigia alternans of Halbey must be considered as a peripheral angioneurosis, and is discussed in the section on blood vessels.

In general it may be said that those questions which have been of great interest in the last decade, questions of the relation of the vago-sympathetic system to pulse irregularities, to the Stokes-Adams syndrome, the functional adynamias, and the organic disturbances in the atro-ventricular structures are still far from a satisfactory solution. If. as Ciechanowski says in his monograph upon the heart, one regards the discovery of the atro-ventricular system as a new chapter and a new page in the many-sided book of cardiac pathology, one must admit that the researches up till now are scarcely more than outlined, the ABC of the new chapter.

14. *Blood Vessels.*—The nervous regulation of blood vessels, arteries (Stilling), veins (Glotz) and capillaries (Steinach) has been recognized for many years. Only the nature and site of the vasomotor organic disturbances in the central and peripheral nervous systems are as yet possible of diagnosis. More often the opposite path of reasoning is taken in that the anatomy and physiology of blood vessels yields information about clinical and pathological conditions.

The following facts contribute to the difficulties in clarifying the activities of the vasomotors.

1. First of all, the relations of the vasoconstrictors to the vasodilators and the relations of both to the heart and its ganglia have not as yet been cleared up. According to many physiologists vasoconstriction follows active stimulation, vasodilation, active inhibition of the circular muscle of the blood vessels.

2. Secondly, it is not definitely known whether or not the vasodilators and vasoconstrictors follow the same paths, and further whether vasodilator changes plethysmographically recorded are due

to a diminution of the tone of the vasodilators or to stimulation of the vasodilator fibers.

3. Thirdly, the situation is complicated by the fact that the innervation of all blood vessels is not always simultaneous and of equal intensity. It is not proper either teleologically or physiologically to suppose that all blood vessels should contract or dilate simultaneously and should thus suddenly throw an excess of blood into or remove an excess of blood from the heart. In this regard it may be said that the visceral blood vessels act individually and in most instances both the external and internal blood vessels of the heart react oppositely to those of the extremities (Wiechowski, Hürthle, Weber).

4. Finally, another difficulty is the fact that the influence of the sympathetic nerves upon the blood vessels is not only exerted upon the smooth muscle of the arteries but also affects the muscle cells of analogous nature in the capillaries (Rouget, Mayer, Steinach, Kahn).

The question is, what may be learned as to the localization of vasomotor centers and tracts in the periphery, cerebrospinal axis and cerebral cortex by a study of anatomy, physiology and experimental pharmacology.

The skin vessels of the face are supplied by fibers from the upper cervical ganglion. They pass via the internal carotid plexus to the gasserian ganglion, the spinal ganglion of the trigeminus. From here they pass with the fibers to the sweat glands via the sensory nerves to the face. The fibers to the vascular supply of the extremities pass via the plexi to these parts (Duval, Benders, Claude Bernard). The vasomotors to the arm go via the brachial plexus and arise in the thoracic part of the sympathetic chain. The vasomotors to the leg which go via the sciatic nerve arise in the lumbar cord. The former group arises much lower, the latter much higher than the corresponding spinal motor nerves and must therefore be fairly near to one another in the spinal cord. Helweg places the segmental origin of the vasomotor fibers to the arm at C5–D7, the majority arising from D3–D7. Langley found that the vasoconstrictor fibers of the upper extremities arose in segments D4–D10. Those for the lower extremities in D12–L3. The former ascend in the sympathetic chain, the latter descend. According to the contention of Onuf and Collins, the fibers for the upper extremities have their origin in segments which are lower than those at which the fibers leave the spinal cord. Thus they ascend not only in the sympathetic chain but also in the spinal cord. The same is claimed

for the lower extremity, only here the fibers descend in the spinal cord and then leave at segments below their origin to descend further in the sympathetic chain before going to the peripheral nerves.

The principal control lies normally in the cerebrospinal axis. However, when this is vitiated by destruction of the cord or section of the peripheral nerves, peripheral tone comes to the rescue. After a short period of vascular depression the reserve tone, arising most probably in the peripheral ganglia, reëstablishes the normal level of pressure. In general the spinal cord serves local segmental functions. The bulbar or main center of blood pressure behaves differently. This lies in the nucleus dorsalis vagi and is the autonomic vascular center of nearly all the viscera. It may be stimulated reflexly from many points. If the bulbar center is stimulated by one means or another, autonomic stimulation of the vessels in the splanchnic area results with dilatation of the vessels and subsequent narrowing of the peripheral vessels. The depressor nerve in the aorta guards against too great a rise of blood pressure, for it is reflexly stimulated by any increase in aortic pressure (Tschermak).

According to some authors (Benders) the bulbar center owes its control of the large vasoconstrictor areas to the presence of paths which run to the lower spinal cord centers and which are secondarily stimulated when the bulbar centers are stimulated.

That the cerebral vessels are controlled by a center lying above the bulbar center is natural from their position. If the superior cervical ganglion be nicotinized, thus cutting the path of the vasoconstrictor nerves, constriction of the verebral vessels cannot be obtained. Vasodilatation in the brain may still be produced and also after destruction of the medulla oblongata. Weber states that there are both vasodilator and vasoconstrictor fibers for the cerebral vessels in the cervical sympathetic.

Some authors deny, others affirm the presence of a cortical center. Experiments in which the frontal brain area in cats is stimulated with resultant stimulation of the splanchnic area and increase of blood pressure (Lewandowsky, Weber) have been cited as evidence of a center.

The following course of the vasomotor tracts in man has been suggested. The evidence is clinical and experimental. Frontal lobes (Rossolimo), internal capsule, nucleus caudatus, thalamus (Bechterew), pons, gray matter of the fourth ventricle, in the region of the calamus scriptorius (Reinhold) of the medulla oblongata "weisse Dreikantenbahn" (Helweg) or anterior lateral tracts (Cassirer) and the gray lateral horn of the spinal cord. Helweg states that

almost all the vasomotor paths cross in the posterior commissure. The further course of the vasoconstrictor fibers is the customary one; anterior root, communicating branch, sympathetic ganglion. The autonomic vasodilators pass through the posterior sensory roots (Stricker).

The following observations indicate that the vasodilator and pain fibers take the same course: (*a*) Stimulation of sensory fibers causes both pain and cutaneous hyperemia; (*b*) paralysis produces anesthesia and cutaneous anemia. Certain pathological conditions as meningitis add to the proof, for there occurs simultaneously increased irritability of the sensory nerves (hyperalgesia) and of the vasodilators (dermatographia). After experimental section of the posterior roots, Bruce found absence of the initial hyperemia of the inflammatory reaction in the corresponding skin area, an evidence of stimulation of the dilators.

The diagram of Rudzki-Hornowski, based upon the work of Ranvier, Schiff and Gianuzzi, shows the course of the vasoconstrictor fibers in the periphery. According to these authors there is a layer of ganglion cells in the adventitia. From these, fine fibers pass to a new plexus in the media. The fibers from this plexus end in the musculature of the media, *i. e.,* in the elastic, radiate muscle fibers of Dürck or in the intima.

Most of the peripheral vasomotor manifestations are reflex in character, the sensory stimulus going to the spinal cord. We must recognize that a vasomotor reflex occurs in this way as any other reflex activity, as tendon or skin reflexes. A sensory stimulus goes to the spinal cord, the stimulus is now carried to another cell and thence to the motor tract. It is thus possible to divide the disturbances of vascular reflexes according to the location of the causative trouble—

1. Disturbances of the sensory part of the arc.
2. Disturbances of the motor part of the arc.
3. Disturbances of both parts of the arc.
4. Disturbances of the central influencing paths not part of the arc.

According to Langley, vegetative nerve cells cannot of themselves cause true reflexes. The intervention of the central nervous system is necessary to their production.

Under normal conditions the vessels are in a state of medium fulness due to the normal simultaneously acting, antagonistic inner-

vation of the dilator and constrictor nerves. This causes the normal color of the skin. Just where the endogenous vasotonic hormones act, upon vessel musculature or nerve endings, is still not finally settled. The nerve endings are most probably the site of action, in spite of what we know of the action of barium upon vessel musculature, and of antimony upon capillaries.

Physiological variations in the tone of the vessels of the skin occur as soon as there is a flow of blood to or from—

1. The brain .....Sleep. Emotions.
2. The stomach .....Height of digestion.
3. The periphery .....Exercise. Overheating.

Gradual variations are found in individuals with increased irritability of the vascular system (neurasthenia). This manifests itself as dermatographia or exudative wheal production following energetic skin irritation. Reversal of this reaction—local anemia following skin irritation, general pallor after overheating the body—are rare occurrences.

Vasomotor disturbances play a large part in clinical pathology, but their diagnostic value for localization is limited. This is because we do not know the location of all the various vascular centers in man, nor the vicarious activities of each of the three main centers in cases where there are lesions of one or another.

Many authors believe that there exists an antagonism between the bulbar autonomic centers and the spinal sympathetic centers, similar to that existing for the eye, the lachrymal and the salivary glands. This theory assumes that where the autonomic has any influence, it is vasodilator, while the cervical sympathetic acts as a constrictor. Pharmacological experiments bear out this theory of the antagonistic action of the two vasomotor areas.

The usual bases for conclusions give no clue as to the site of central angioneurotic disturbances. Nor do the results of pharmacological investigations (vasotonic, centrally acting drugs), nor do accessory symptoms as the initial pallor of an epileptic attack, or the skin hyperemia in capsular, pontine or bulbar hemorrhages.

Nor is the situation much better as regards the genesis of peripheral hyperemias and anemias.

1. Stimulation of the vasodilator fibers seems to be responsible for the "tonic hyperemias" in neuralgia, neuritis, febrile, toxic and infectious erythema and for certain vasomotor neuroses of the skin as erythromelalgia with spontaneous pain (Weir Mitchell) and erythromelalgia with hyperidrosis and hyperalgesia without pain

(Hess-Koenigstein). When erythema follows long-standing cyanosis, there is transudation with stasis following slowing of the blood-stream due to vasodilation. The above-mentioned clinicians in connection with the mechanism of all these states of vascular dilation justly call attention to the newer work of Schwarz and Lemberger. These authors showed that very small amounts of acid in the blood give rise to vasodilatation. They claim that diabetic acidosis as well as the acidosis of fever and severe abdominal disturbances may serve as explanations of the accompanying erythema.

Some authors, Kretschmer and Kleissel, maintain that there is a diminution of the alkalinity of the blood in sympathicotonic individuals. Adrenalin is therefore destroyed more slowly, accumulates in the blood and stimulates the sympathetic system. Under the heading "spastic anemia" due to lasting vasoconstriction of the smallest vessels are to be included all conditions in which, though the color index of the blood is normal, there is an apparent anemia. Among these conditions are pseudo-chlorosis, chronic nephritis, malaria, tropical anemia and neurasthenia. Hess and Koenigstein include pseudosclerosis (Schlayer and Fischer) in this group. In this condition sclerosis is simulated by the vascular spasm.

Those conditions which are purely paroxysmal are also considered of nervous origin: (1) Hemicrania with angiospastic anemia of the corresponding half of the head; (2) asphygmia alternans (Halbey) in which the radial pulse is absent on side; (3) the vasomotor neurosis of Nothnagel with pallor, coldness, and absence of feeling in the affected extremity (doigts morts); (4) Raynaud's disease; (5) intermittent claudication either of the vessels of the periphery or the viscera, the arteries being in some cases normal, in others sclerosed. The pain accompanying this condition is due to stimulation of the fibers and ganglia in the blood vessel walls.

The vasomotor disturbances occurring in Czerny's exudative diathesis of young children, the vasotonic symptom complex of Hamburger in young adults and the vagotonia of the blood-vessels occuring in elderly men (Eppinger), all seem to belong to the same group. They may be summed up as vasoneurosis which manifests itself as a regional paroxysmal anemia of the vessels of the brain, heart, face or extremities accompanied by transitory fainting, precordal pain, pallor of the face, and coldness of the hands and feet.

Intermittent intestinal claudication or dyspragia is according to Hess analogous to these vascular crises of the skin. It occurs, however, in the internal organs. The various types are: (1) Paroxysmal constriction of the intestinal vessels (Ortner, Schnitzler); (2) spasm

of the renal vessels following sensory stimulation, the dyspragia renalis of Huchard; (3) spasm of the coronary vessels, the angina pectoris vera and vasomotoria of Nothnagel; (4) all the visceral pains associated with rise in blood-pressure, included by Pal under the general heading of *vascular crises*.

Clinically we have made the error of becoming accustomed to attitude all vasomotor symptoms to overt or underfunctioning of the vasoconstrictors.

The example of typical paralysis of the vasoconstrictor nerves is erythromelalgia. The example of typical spasm of vasoconstrictor nerves is Raynaud's disease or angiospastic gangrene and "dead fingers." The example of typical hyperirritability of vasomotor nerves is acute angioneurotic edema (Quincke) in all the varieties either of the skin or mucous membranes, periodic hydrarthrosis (hydrops articulorum intermittens), periodic flow of gastric juice (gastrosucchorea periodica), sudden blushing of the youthful either with or without erythrophobia and paroxysmal pallor accompanied by a functional ischemia of the head.

So much for the vasomotor neuroses "sensu strictiori." The occurrence of vasomotor symptoms accessory to diseases of the brain, spinal cord and periphery is very frequent.

The simplest example of a vasomotor abnormality of peripheral origin is that due to mechanical or functional paralysis of the cervical sympathetic on one side. As a result there is unilateral vasodilation of the face. This is not constantly present. The peculiar inconsistency is possibly explicable by incompleteness of the lesion, mixing of stimulation and paralysis or by the experimentally proved hyperirritability of the peripheral part of sympathetic nerves following section.

In disease of the cortex, Jacksonian epileptic attacks are accompanied by severe vasomotor manifestations, pallor or redness.

In cerebral hemiplegia there is not unusually a lowering of pulse-rate, blood-pressure and temperature as well as edema upon the affected side at the beginning of the disease.

Just how the initial hyperemia due to paralysis of the vasoconstrictors is replaced by coolness and pallor is not definitely known. If the degree of muscular paralysis paralleled the definite residual vasomotor anomaly, this latter could be ascribed to the inactivity of the paralyzed muscles and to the consequent venous stasis and diminished production of heat. Where this parallelism fails to be present, one feels that the bulbar center becomes accustomed to regulate vasomotor activity uninfluenced by the central neurone.

It is probable, that in vasomotor anomalies of spinal origin, neighboring vasomotor centers act vicariously, and replace the centers which are out of commission. In the early stages of myelitis and tabes dorsalis the vasoconstrictor fibers are stimulated as the marked pallor and subjective feeling of cold indicates.

In many respects, clinical data coincides with the results of experimentation. Up to now our knowledge is almost entirely derived from investigations on animals. There have been, however, investigations on the degree of vasomotor reaction following stimulation of healthy and diseased parts. Biach and Bauer have shown that if a normal extremity is cooled, its temperature falls, first, due to a purely physical removal of warmth, and, second, due to vasoconstriction with a resultant, poorer blood supply. This vasoconstriction is due on one hand to the direct effect of the cold upon the ganglia in the walls of the blood-vessels, on the other, to reflex central vasoconstrictor stimulation. It follows therefore that under normal conditions, there is a greater fall of temperature in general biological reactions than can be accounted for by the strictly physical influences. At any rate, an excessive loss of warmth is avoided in this way.

In those cases where there is paralysis of the vasomotors, the reflex vasoconstriction with its resultant cooling is absent, and thus the skin temperature falls less than under normal conditions. Corresponding to this Biach and Bauer have found in hemiplegics that the paralyzed side is cooled less than the healthy side. This does not always hold, since there are also cases in which, in spite of diminished vascular tone, there is no abnormal reaction of the vasomotors, and cases in which, in spite of equal temperatures, before the experiment there is a slight drop in the affected limb, showing that there exists some disturbance of the vasomotors.

The animal experiments of Freund and Strassman upon the spinal cord show how great the control of general body temperature by the vasomotors really is. After section of the cord in the dorsal region there is immediate paralysis of the vasomotors with a general drop of body temperature. The organism seeks to neutralize the loss of heat by an increase of the internal metabolism, provided the room temperature remains between 18° and 31° C. Temperature regulation is greatly disturbed and the animals become cool if their loss of heat is not diminished by being wrapped up or by raising the external temperature. Section of the cord in the cervical region causes the animal to lose the power of regulating temperature either physically or chemically. Its body heat is only retained at a normal

level when the external temperature lies between 28° and 31° C. When the external temperature becomes higher or lower the internal temperature of the vasomotor-paralyzed animal varies considerably.

The plethysmographic observations of Stursberg on patients with normal spinal cords and on those with spinal cord diseases are of distinct practical value. These observations have shown that if one forearm is cooled, the plethysmographic curve of the other arm sinks, while it rises if the feet are cooled. They show furthermore that section of the cord in the mid-dorsal region in man causes a marked disturbance in the innervation of the skin blood-vessels. The vessels are divided into two separate areas. The vessels of the upper half act differently from those of the lower. This is of course not so in the normal individual. This is shown by the fact that upon stimulation of the feet the vasoconstrictor action is found only in the lower limbs, a limitation not normally found. The vessels of the upper half are affected in the opposite fashion. This is due probably to a passive distention of the vessels due to a general increase of blood-pressure.

These same experiments have shown that the vasocontrictor fibers for the upper extremities arise from the spinal cord in man above the seventh thoracic segment. They also show that the nerve fibers which carry the sensory stimuli from the lower extremities to the vasoconstrictor fibers of the upper extremity, also pass through the seventh thoracic segment. Thus the coördination of the vasoconstrictor control of the upper and lower halves of the body lies in this center of the spinal cord. These observations do not differ materially from the older ones, according to which the upper extremities received their vegetative fibers through the roots of the fourth to tenth thoracic nerves, their rami communicantes passing through the ganglionated cord and the stellate gangloin to the brachial plexus, or as Claude Bernard believed through the sympathetic to the arm vessels without the assistance of the brachial plexus.

The Mosso-Lehmann plethysmograph gives the most precise information regarding the large movements of the blood volume resultant upon psychic activity, changes in cardiac activity or the state of contraction of the blood-vessels. The best method of obtaining information about all vasomotor activities is by combined measurement of the volume of the arm and the abdomen (Fig. 8, *a, b*).

If the cause of the vasomotor change be a change in the heart beat then according to Weber there must be equal increase in volume in all other parts of the body. If a vasoconstriction be the cause, there must be an increase in volume in some other part of the body,

in this case most probably in the abdominal organs. If this was not the case active dilatation of the measured blood-vessels occurred.

A closer study of the separate results of the investigation of the normal movements of blood during psychic activity may be accomplished with the help of the table arranged by Weber. Many noteworthy facts may be gained from it.

	Brain.	Ext. Parts of the Head	Abdominal Organs	Extremities and Ext. Parts of the Trunk
During movements	×	−	−	×
During mental work	×	−	×	−
During fear	×	−	×	−
During a pleasant feeling	×	×	−	×
During an unpleasant feeling	−	−	×	−
During sleep	×		−	×

× = increase, − = decrease of the volume of blood in the part referred to.

The following conclusions may be drawn:

1. The blood-vessels of the brain act exceptionally to those of the rest of the body.

2. It is controlled by a separate vasomotor center, as has been stated above.

3. During unpleasant feelings there is dilatation, during pleasant, constriction of the abdominal vessels. Thus there is movement of the blood volume from within to without during pleasant feelings, and from without to within during unpleasant feelings.

4. Sudden and conscious feelings of pain cause vasodilatation of the blood-vessels of the face.

5. Emotions (joy, shame, anger, sorrow) cause changes in the vasomotor innervation of the face and skin over the skull.

It is worth adding that the flow of blood into the extremities during activity of the part is not entirely a mechanical result of the movement, but is doubtless also correlated to mental activity. (*a*) the flow of blood takes place when the other hand is moved; (*b*) the same effect is brought about if no movement is made, and only a suggestion of a movement is made during the hypnotic state; (*c*) the flow of blood into the extremities is absent if only passive movements of the extremity are made.

Profuse general or local sweating and mild cyanosis of the peripheral parts are signs of vagotonia in which the tone of the vasodilator autonomic is increased. In vagotonics urticaria occurs in conjunction with eosinophilia and increased tolerance to adrenalin and carbohydrates.

The most thoroughly understood of the pharmacological substances is adrenalin, the physiological secretion of the adrenal glands and of the chromaffin tissues. Its vasotonic action has been much studied in recent years. Since its discovery it has been widely used therapeutically in infections, sepsis, nervous asthma and collapse (Gaisbock). The dose has been ½ to 1 mg. either intravenously or subcutaneously. The direct action is a rapidly beginning rise in blood-pressure due to vasoconstriction, which disappears after a few minutes either because of fatigue of the vascular walls or because of a simultaneous stimulation of the vasodilators. The rise in blood-pressure, which may be 50 per cent. to 100 per cent. of the normal, usually follows an initial tachycardia, which is followed by a bradycardia. Continuous injection of adrenalin causes the blood-pressure to remain high, but the intensity of the action depends as a rule not upon the absolute amount of adrenalin but upon the difference between the concentration of the injected fluid and the blood.

If one disregard the stimulating effect of adrenalin upon the heart one can attribute the rise in blood-pressure mainly to the narrowing of the smallest arteries. The place where the adrenalin acts is at the periphery, as may be shown on one hand by experiments in which excised pieces of blood vessels bathed in adrenalin become smaller in cross-section, and on the other by clinical observations upon cases with central paralysis of the vasomotors (traumatic injury to the cervical spinal cord, pharmacological paralysis of the bulbar centers by poisoning with chloral hydrate) in which the great lack of vascular tone and the great fall of blood-pressure are quite dissipated by the use of adrenalin.

The greatest action of adrenalin is upon the aortic vessels and upon the splanchnic vessels, in which the largest part of the blood is contained. By their contraction the blood is forced from the splanchnic vessels mainly into the lungs and heart. Some groups of vessels show consistent variation from the usual action of adrenalin. This is of clinical significance. Occasionally neighboring vascular regions act oppositely (tongue, lip). The heart vessels (Art. coronariæ), which probably receive their constrictors from the vagus and their dilators from the sympathetic, always dilate under the action of adrenalin; less constant in action, but usually atypical, is the action of the vessels of the brain and lungs.

The kind and nature of the susceptibility of the end-organs to the stimulation of adrenalin shows many variations. These, as has been shown above, depend partly upon the nerve tone, partly upon

the irritability of the nerve-endings, partly upon the condition of the organ itself, partly upon the various conditions caused by both biological and pathological changes, changes which have been established by the general principles of modern pharmacodynamics. Thyroid extract, a vasotonic hormone, has but little effect upon the vasoconstrictors. Contrary to the action of adrenalin is that of the autonomic drugs. These stimulate the dilator fibers of peripheral blood vessels, an example of which is the reddening of the face or of the entire body under the action of pilocarpin.

The question of the relation of trophic disturbances to those of the vasomotors is not yet very clear. The trophic function of nerve tissues does not originate in specific centers or pass outward in specific nerve paths, but has its reflex path in the same path as is used by other functions.

The descending branch of this path is made up of the vasomotor fibers. Disturbances of these never lead to trophic disturbances, but to simple vascular paralysis, which leads to pathological changes in the vessel-walls only after a considerable time.

It is well known that the skin, subcutaneous tissues, muscles and bones are not equally involved in Raynaud's angiospastic gangrene. From this Phelps draws the conclusion that the above mentioned tissues have separate vasomotor-trophic centers in the central nervous system. Benders justly states that the fact that the resistance of the above mentioned tissues as well as their irritability is very unequal must not be lost sight of. It is known that stimulation of the gray rami communicantes (Langley) produces a greater reaction in the skin vessels than in the deeper vessels. It is also known that stimulation of the vasomotor centers produces the strongest reaction in the smallest and most distant blood vessels.

Disturbances of pigmentation are found in the most varied of physiological conditions, in which local or general trophic abnormalities occur. This symptom may be found not only in Addison's disease, but also in a number of other nervous diseases (Graves' disease) in which autonomic stimulation may be assumed. Konigstein recently has shown a relation between pigmentation and autonomic stimulation by experiments upon adrenalectomized dogs and adrenalin-fed frogs.

15.—*Sweat Glands.*—There remain finally for discussion, disturbances of the activities of the sweat glands, disturbances which often accompany vasomotor abnormalities. The occasional difference between vasomotor and secretory disturbances in diseases of the spinal cord makes it necessary to assume a different localiza-

tion in and near the lateral horn for the vasomotor and secretory centers. Pharmacological experiments show that substances which stimulate the autonomic system affect both the vasodilator and the sweat gland fibers (hyperemia and hyperidrosis). Physiological and clinical observations show on the other hand that erythema with marked arterial dilatation occurs without increased sweating and that on the other hand marked secretion of sweat occurs in the general or local anemia of such conditions as the death agony, fear, ligature of the artery of an extremity, etc. Clinically speaking, sweating and vasodilatation are not therefore dependent upon each other. Anatomical and pharmacological observations do not agree, for the former places the nerve control of the sweat glands in the sympathetic, the latter in the autonomic.

More exact experiments of recent date point to a double innervation of the sweat glands; from the cervical sympathetic and the bulbar autonomic.

All that has been said above about the tracts concerned in vasomotor disturbances may be transferred to apply to the sweat gland fibers, both in their central and peripheral course. Animal experiments (Winkler, Gribojedow) and observations in man indicate that there are sweat centers in the brain; marked unilateral sweating in motor hemiplegia indicated that the central sweat tract lies close to the motor fibers in the internal capsule and like it, decussates (Binger and Burg).

The sweat fibers have their peripheral course like other vegetative fibers, *i. e.,* with the sensory fibers, and sweat anomalies are more frequent with sensory disturbances than with motor. Romberg knew that a transplanted nose did not secrete sweat until its sensation had returned (Cassirer).

Charcot placed the sweat centers in the spinal cord beneath the posterior horn near the lateral horn, while Adamkiewicz and Biedl placed them in the lateral group of ganglion cells in the anterior horn. The fibers are supposed to pass by way of the anterior roots to the sympathetic chain. The fibers for the fore-paws of the cat pass by way of the fourth to ninth dorsal nerves, for the hind paws by way of the lower dorsal nerves and the upper four lumbar nerves, for the face by way of the second to seventh cervical nerves (Langley, Nawrocki). The sympathetic fibers to the face pass therefore from the cervical cord centers to the superior cervical ganglion to the carotid plexus and then to the Gasserian ganglion from which they pass with the sensory fibers of the fifth nerve to the skin of the face.

L. Muller believes that the contention that sweat fibers run in the peripheral facial nerve (Köster) must be definitely abandoned. Autonomic sweat centers do exist in the central part of the facial nerve (occasional sweat anomalies in rheumatic paralysis of the nuclear part of the facial). The fibers pass thence by way of ramus communicans albus of the facial and the N. petrosus superficialis major to the sphenopalatine ganglion. From here they pass outward with the fibers of the trigeminus, not with the fibers of the facial.

The fact that there is an autonomic innervation besides the sympathetic is shown by the possibility (Dupuy) of stimulating the sweat glands to activity in animals even after the sympathetic fibers have been cut.

As regards the nervous anomalies of sweat secretion in organic diseases the following may be mentioned: Marked sweating in hemiplegia, which has already been mentioned, hyperidrosis in herpes zoster, anidrosis in those parts paralyzed in anterior poliomyelitis, syringomyelia, multiple sclerosis, myelitis and tumors of the spinal cord. Occasionally in several members of a family there is circumscribed sweating of the face after smelling or chewing certain sharp substances which seems to be a subsidiary reaction. Hemihyperidrosis or hemihydrorrhea is sometimes regarded as a manifestation of mental degeneration. It is accompanied by pupillary and cardiovascular changes. Many authors regard it as a sympathetic neurosis, others think it a separate and isolated manifestation of defective body development.

In the functional condition "vagotonia" there are localized as well as general attacks of sweating, moist hands and hyperirritability to pilocarpin. The slightest mental excitement, as embarrassment, fear, waiting, will produce sweating in "vagotonics." Just as anxiety brings sweat to the brow, so do severe psychic and physical pains and the specific, sensory, peripheral stimuli (heat and pressure). These latter stimuli are known to be the activators not only of the sweat glands but also the neighboring blood vessels and pilomotor muscles.

Veraguth's psychogalvanic reflex phenomenon shows how very delicate, even more delicate than the pupillary reaction, the reaction of the sweat-apparatus to psychical stimuli really is. The experiment consists in putting the patient in the course of a galvanic current (Veraguth's mirror galvanometer or Einthoven's string galvanometer) and observing the variations in the strength of the current. This electrically obtained curve is an extremely delicate

indicator of the more or less complete balance of the emotional condition of an individual. The variations following all varieties of endosomatic events all show the common characteristic of a latent period of several seconds after the event has begun. This implies that the process is rather physiological than purely physical. After these electrical manifestations were shown to be parallel to the reflex, and consistently followed the same psychic stimuli, Veraguth named them the "psychophysical galvanic reflex phenomenon" or more briefly the "psychogalvanic reflex." The greatest reaction to any of the stimuli tried was found to be to a complex whose emotional tone was great, which had the power to evoke the greatest affective response. An example is a patient of Moravcsik's, who, when a number of names of streets were recited to him, showed the greatest reaction when the street on which his sweetheart lived was mentioned. This same author states that there are doubtless individual variations in the latent period. These variations are not only of form, but also of amount. Besides, even though the constancy of the foreign current can be easily controlled, there is a considerable influence exerted upon amount and quality of the deviations of the needle by the condition, surroundings, emotional state, and other exo- and endopsychic factors affecting the person experimented upon. It is therefore wise to establish the average, individual reactibility in each case.

These electrical variations show graphically that a current passing through the body via the hands shows variations after mental exertion, and after sensory and psychic stimulation. *These variations are in all probability due to changes in the innervation of the sweat glands of the palm of the hand, or, more particularly, to the changes in moistness of the hands.* The fact that dogs who have no sweat glands also show the Veraguth reaction must not be forgotten, however. Gregor states that in hysterical, hypnotic and organic anesthesias the reflex is absent.

The finest variations in the mental balance are mirrored by the continually changing resistance of the skin.

16. *Pilomotor and Other Smooth Muscles of the Skin.*—The pilomotor and smooth muscle of the skin, according to anatomical data, receive their innervation mainly from the sympathetic system. Rynbeck's experiments upon cats showed that the hair-raising or pilomotor nerve fibers run in the peripheral sensory nerves and supply corresponding skin areas. The sensory and motor innervation of the skin are both segmental. Fibers from about five sympathetic ganglia run in every spinal nerve.

Various stimuli bring about a contraction of the smooth musculature of the skin. The following are examples: Mechanical: dull and sharp sticking; thermic: pieces of ice and thermophors; electrical: gardually increasing faradic and galvanic currents. Goose-flesh, which is due to the activity of the erectores pilorum, and which may best be seen by oblique light, is very readily produced by local application of cold and occasionally by fine long-lasting folding of the skin.

The spontaneous and characteristic feeling as if one's hair stands on end is occasionally accompanied by a feeling of cold. That this is due to vasoconstriction can be shown in areas not having any pilomotor muscles. The stimulus which causes contraction of the pilomotor muscles also causes vasoconstriction, since the anatomical path for both has the same origin and the same topographical destination.

This common path has been demonstrated by Mackenzie in the following experiments. If the skin of a suitable person is vigorously rubbed with a piece of flannel just beneath the nipple one can see goose-flesh appear on the rubbed place and slowly spread upwards to the clavicle and further to the inner aspect of the upper and lower arm. At the same time the patient feels a remarkable sensation of cold passing up the chest and over those aspects of the arm which correspond to the areas with goose-flesh. The basis for this distribution lies in the fact that the rubbing sends stimuli to the spinal cord centers for the pilomotor and vasoconstrictor nerves. These spread upward. This may be assumed from the fact that the pupil dilates at the same time, and the pupil receives its dilator fibers from the upper thoracic nerves of the spinal cord. In one case of Mackenzie, the patient felt a sensation of cold in the cheek and Sherrington has shown that stimulation of the sympathetic fibers from the third thoracic nerves in monkeys will cause erection of the hair of the cheek. The same author has shown that stimulation of the upper sympathetic in monkeys and cats will cause erection of the hair between the eyes and ears as well as in the occipital region. Langlet in analogous experiments found circumscribed contraction of the hair muscles on the back of the cat, Kahn, on the tail of the marmot, Jegorow, movement of the head-feathers of the turkey.

In human pathology, taking cold water into the stomach is followed by a feeling of cold in the abdomen which is probably due to a constriction of the adjacent skin vessels, and is accompanied by a circumscribed area of "goose-flesh."

The pilomotor reflexes which occur unilaterally in nervous people are worthy of note. They accompany various internal diseases

and are limited to a circumscribed area determined by innervation. As an example, direct mechanical stimulation of a branch of the pudendal plexus (prostatitis, cystitis, rectal examination) will produce a circumscribed area of goose-flesh corresponding to some area supplied by the motor part of the lumbar plexus. These nerves to the skin carry, according to Pinkus, the sympathetic nerve-fibers to the erectores pilorum with them, fibers which compose part of the reflex arc. The above-mentioned motor reflex is comparable to the other reflexes of the skin which are brought into play in disturbances of skin innervation. Up to now we have only recognized skin reflexes occurring in disturbances of the sensory, secretory and vasomotor functions. The pilomotor reflex must be added to these. Various stimuli, particularly electrical, applied at certain places, as for example the lateral cervical region (Koenigsfeld and Zierl) and the nape of the neck (Sobotka), will produce, besides the local and long-lasting reaction which manifests itself in a stimulation of the piloerectors, a true secondary reaction of wide extent. This spreads through the spinal cord and the sympathetic ganglia and manifests itself as goose-flesh having a unilateral distribution. When the stimulating electrode is placed under the vertebra which lies at the juncture of the sternocleidomastoid and the trapezius muscles, the stimulation may be said to be applied directly upon the cervical sympathetic.

If rapidly repeated stimuli are applied there is a gradual weakening and finally cessation of the reaction (saturation or fatigue reaction). If a neighboring area of skin is now stimulated the reaction promptly recommences. The stimulation may be simply a slight folding of the skin.

It may furthermore be said that the rising of hair follicles is not necessarily associated with the production of pain and that thermic stimuli do not always bring with them the subjective feeling of cold nor always imply the presence of an anemia of the skin, as the observation of goose-flesh in febrile scarlet fever cases when either ice or heat is applied (Koenigsfeld). The reflex acts only upon the erectores, not upon the vessels, even though the vascular reflex does give some support to the other.

Section of the nerves of the skin leaves local pilomotor activity uninfluenced, which explains the fact that goose-flesh never crosses the midline of the body.

There is also smooth muscle in the tunica dartos and in the nipple, which contracts in sexual excitement. Of more importance in this connection is the smooth muscle in the skin of the penis which

is innervated and made to contract and relax simultaneously with the muscles of the erectile bodies (vasoconstrictor fibers) by means of the dorsalis penis nerve. This coördination plays a considerable rôle in the mechanism of erection and of detumescence caused by cold and the action of unpleasant emotional states.

What has been said of the antagonistic innervation of the sweat glands may be applied to the pilo-erector muscles. Upon anatomical grounds they are only innervated by the sympathetic, while upon pharmacological grounds (intravenous injection of adrenalin) they seem to be innervated by the autonomic.

Among the rarities found in human pathology may be mentioned the "trichopilous" crises of tabetics (Neumann) and the unilateral crises of hemicrania (migraine) (Féré).

As to the psychic influence upon pilomotor nerves, this much may be said; that it is quite strong. Goose-flesh with a feeling of cold may be produced by very lively suggestion of general or unilateral cold as well as by certain unpleasant sensations, as scratching upon a slate table or a pane of glass or grinding of teeth. It may also be associated with intense emotional states, ecstatic or depressive.

17. *Endocrinous or Intrenal Secretory Glands.*—A few words must be said at the close of our observations concerning the mutual relations between the vegetative nervous system and some of the glands of external and internal secretion and of digestion. This subject will be discussed only in those aspects which have not been emphasized in the general section or in the sections on special organs.

The important physiological conception of the significance of the circulation of the blood in the body has led to the knowledge that this phenomenon serves, among other purposes, that of the exchange of the nutritional and waste products of the body, and that of giving the material for the special secretions of those organs which receive their stimuli to activity from the nervous system. But it has also been discovered that in addition to activation by the nervous system, there is an activation by means of substances circulating in the blood. These substances act directly upon specific organs, or influence their reactivity by acting upon their nerve supply.

The proof that these substances or hormones give the specific stimulus was obtained by finding the same results after as before section of the nerves to the organ.

We have on the one hand organs which have a rich blood supply, but no external means of emptying their secretions, and which supply substances directly to the blood, while on the other hand we have organs which, though they do the same thing, have also an external secretion. These are the testicle, ovary, pancreas, stomach and liver.

Under special conditions, hormone production may be influenced by the nervous system, as, for example, in the "piqûre."

As Köhler has justly observed, we must conceive of all hormones as being constantly produced, and as being constantly present in the blood stream. Further that they all have an influence upon each other so that there exists in the healthy body an equilibrium between their stimulating and inhibitory effects, *i. e.*, a normal hormone tone, a balance whose maintenance is one of the most delicate chemical arrangements of the body. If the normal amounts of hormone act as physiological stimulants, we may readily see that disease in any of the organs producing them will cause a dystrophy. There will ensue a production of too much of the hormone (hyperfunction), or of too little (hypofunction). Following soon upon this disturbance of one gland, there will come a disturbance in the functions of several glands, since, as we have seen, the individual glands are mutually related in the rôle of stimulators or substitutes of each other. Thus we get a condition of polyglandular dystrophy.

A roughly schematic division of the glands according to their effect upon metabolism follows:

1. Acceleration: Thyroid, Hypophysis, Adrenal, Sex Glands.
2. Retarding: Parathyroid, Pancreas, Thymus.[1]

The first group stimulates the sympathetic, the second inhibits it, facts which may be observed in all conditions of hyper- or hypofunction of the glands.

It has been found in metabolism experiments that protein, fat

[1] *Translator's Note.*—Falta, in his book "Die Erkrankungen der Blutdrüsen," 1913, gives the following classification:

1. Accelerator [catabolic-dissimilator].
   (*a*) Thyroid.
   (*b*) Hypophysis [posterior lobe].
   (*c*) Chromaffin Tissues.
   (*d*) Sex Glands.
2. Retarding [anabolic-assimilator].
   (*a*) Parathyroids.
   (*b*) Hypophysis [anterior lobe].
   (*c*) Cortex of the adrenals.
   (*d*) Interstitial glands.
   (*e*) Thymus.
   (*f*) Epiphysis.
   (*g*) Pancreas [islands of Langerhans].

Falta states that the thymus and epiphysis probably belong in group 2, the retarding group. As to the pancreas, he says, speaking of group 1: "We may contrast with this group [1] the group of glands [2] with retarding or anabolic, or assimilator hormones. To it belongs the insular apparatus of the pancreas . . . , and further, the parathyroids, etc., etc."

and carbohydrates, as well as many mineral substances, especially calcium, are correspondingly affected (Fr. Müller).

The large glands of the abdominal cavity which, as has been stated before, have innervations analogous to that of the gastrointestinal tract are: the liver, pancreas, adrenals, and kidneys.

(*a*) The liver and pancreas, glands of the utmost import to the body economy, are the only two which the vagus stimulates, the sympathetic inhibits. Without going into the action of adrenalin, cholin and cocaine, we may say that the effects of the "piqûre" in the floor of the third or fourth ventricle may be explained as a result of an injury and stimulation either to the vegetative midbrain tracts or to the dorsal vagus nucleus and its visceral fibers to the liver. There is no doubt of the secretory influence of the vagus. In the discussion of vagotony, the glycosuria and glycemia of liver diseases have already been emphasized.

The spinal cord origin of the nerve fibers for the liver is, according to Hallion, from $D._6$ to $L._2$.

(*b*) The pancreas reacts to the paralyzing effect of atropin upon the vagus, quite like the other salivary glands.[2] The pancreas, like the parotid, yields secretions with varying content of ferments and of varying concentration, according to whether the vagus or the sympathetic fibers are stimulated.

The functional antagonism between the pancreas and the chromaffin tissues, so generally emphasized, has not as yet been conclusively demonstrated. But, as Lubarsch states, we at least may say that the manifestations of a loss of the function of the pancreas are like those of stimulation of the chromaffin system. Whether there be an internal relationship between these two is still entirely unknown. It has not been shown that there is a hyperadrenalemia or any increase in the chromaffin tissues in the body after the pancreas is removed. This would be the least which would have to be shown to make it probable that after loss of the internal secretion of the pancreas a state of hyperfunctioning of the adrenals would follow.[3]

[2] *Translator's Note.*—It must be remembered that the Germans speak of the pancreas as the abdominal salivary gland, "Bauchspeicheldrüse."

[3] *Translator's Note.*—It has been shown by Pemberton and Sweet (Arch. Int. Med., Vol. 10, No. 2) that removal of the adrenals causes a flow of pancreatic juice which may be inhibited by injection of epinephrin, and that this inhibition wears off with the wearing off of the effects of the epinephrin, though more slowly. Whether this be due to vasoconstriction effects, or to some other less understood relations, the authors do not wish to say. However, there is here evidence of a close relation between these two glands.

The relation between diseases of the pancreas and diabetes cannot be considered as being cleared up, since we have come to know of hepatogenous and neurogenous glycosurias as well as glycosurias of other origin, in addition to that due to disease of the pancreas. This is especially true since we have been compelled to give up the idea of some functional disturbances of the pancreas without morphological bases. The readily demonstrable changes in the intertubular cell-groups of the pancreas, such as severe injury or atrophy, lead to diabetes. These cell-groups have been designated islands of Langerhans after their discoverer, and are supposed to yield the internal secretion of the pancreas. Their embryology is as yet obscure. Yet pancreatic diabetes has thus gained a definite pathological basis, which was unknown for many years.

Disease of the pancreas, due to a disturbance of its internal secretion, may, according to M. Cohn, lead to a group of severe symptoms of an autonomic nature. These are exophthalmos, v. Graefe's, Moebius and Stellwag's signs, lymphocytosis, phloridzin glycosuria, dermatographismus, etc.

(*c*) The kidney receives sympathetic vasodilator and secretory fibers from the lower dorsal roots, while, on the other hand, it receives fibers from the vagus which inhibit secretion. The polyuria resulting from "piqûre" is, in all probability, due to a paralysis of the kidney fibers from the vagus nucleus, which ordinarily have an inhibiting action, and whose influence is thus removed.

(*d*) Proof of an internal secretion of the adrenal glands has been obtained by Ascher, by removing all the abdominal viscera except the adrenals, under which conditions, stimulation of the splanchnic nerves will cause a rise of blood-pressure. If the adrenal veins are clamped, this rise will not occur. Lasting nervous stimulation will cause adrenalin to be continuously produced, with effects the same as caused by intravenous injections. Thus, it has been shown that, under physiological conditions, an internal secretion of the adrenalin into the blood takes place.[4]

Some cases of diabetes may be due to over-stimulation of the secretory nerves to the adrenals, whereby an increased supply of adrenalin with ensuing glycosuria results.

[4] *Translator's Note.*—As to the amount of this secretion, Hoskins and McClure (Arch. Int. Med., Vol. 10, No. 2) have shown that normally not enough is produced to influence the sympathetic system, and thus to be a factor in maintaining its normal physiological tone. Only stimuli of exceptional nature will cause enough adrenalin to be produced to affect the sympathetic endings.

In favor of this idea are the facts, stated by Ascher, that the sugar "piqûre" is only active when the adrenals are present, and that emotions may cause an increased secretion of adrenalin into the blood. The fact that adrenalin glycosuria may occur after bilateral splanchnicotomy, and the fact that nicotine cannot produce this, lead Polak to the conclusion that adrenalin itself has a stimulating effect upon the sympathetic nerve endings in the adrenals. All substances which excite the sympathetic, as cocaine and paraldehyd, and all substances which have inhibiting effects upon the sympathetic, as quinine and salicylates, will also inhibit adrenalin glycosuria.

According to Frank, the relations of the chromaffin system to diabetic metabolism, as well as to the high blood-pressure of renal disease, are entirely hypothetical.

What practical rôle the function of the adrenal plays in vagotonia as far as the genitalia are concerned is indicated by the following. In cases with atony of the gravid uterus with consequent inversion or with uterine hemorrhage of doubtful etiology it is usually found on autopsy that the chromaffin system is hypoplastic. In chronic interstitial nephritis a hyperplasia has been found (Neusser, Wiesel). Should physiological adrenalinemia be reduced, due to insufficiency or poor nutrition of adrenals, we may expect to find a decreased tone in the sympathetic nerves to the uterus. If we consider the facts that synthetic adrenalin is less toxic than natural adrenalin and that cocaine increases the reactivity of nerve endings to adrenalin, we may well understand the value in cases which threaten to develop a severe uterine atony and in which natural adrenalin is diminished, of an injection into the uterine musculature of a mixture of synthetic adrenalin and cocaine, or the use of pituitrin or hypophysin, which does not stimulate the uterine nerves, but increases their reactivity.

During the short period of the development of our knowledge of the chromaffin system so many valuable physiological and diagnostic points have been revealed that we may justly await with great interest and expectation the further elucidation of this yet to be completed character of visceral neurology.

(*e*) The thyroid, to which frequent reference has already been made, stands in very close relation to the chromaffin system. The hormone of the thyroid, discovered by Baumann, iodothyrin, has been shown by Oswald to be a combination of two substances, iodothyreoglobulin, containing iodine, and a nucleo-protein, not containing iodine. Of physiological import is the fact that the iodothyreo-

globulin has not only an antagonistic action towards some, synergistic action towards others of the hormones, but also has a great influence upon fat and general metabolism. The gland is a supporter of the adrenals in opposing the pancreatic hormone. The last hormone hinders the organism from being inundated with sugar. When it is absent, its antagonists take the upper hand, whereby the hormone of the adrenals causes a great increase of the sugar in the body, and the hormone of the thyroid causes a great increase in the burning of fat, and in the protein destruction. This occurs even in starvation.

According to many authors (Frank) the relationship between Graves' disease and the sympathetic system is such that the hyperthyroidism stimulates the sympathetic. Thus, the nerves to the adrenals would be stimulated, and adrenalin production would ensue. According to other experimenters (Bauer) Graves' disease is a secondary manifestation, an "internal secretory neurosis," dependent upon increased irritability of the vegetative system.

The clinical pictures of hereditary and congenital hypofunction of the thyroid, as cretinism, myxedema, and of hyperfunction of the thyroid (Graves' disease) are well known, and cause the same manifestations which are produced by paralysis or stimulation of the sympathetic and autonomic nervous system. The behavior of the blood in dysthyreodism is noteworthy (Kocher). In Graves' disease and myxedema there is a percental and absolute decrease of the leucocytes and an increase in the lymphocytes. In Graves' there is a decrease in the coagulability of the blood, while in myxedema there is an increase. Even if the exact etiology of this disease has not been universally shown to be thyreoid, yet the great majority of authors believe it to be such. The conception that the disease is purely a sympathetic disorder unrelated to other causes is more clearly explained by the theory of a hormone, since this also produces a great many symptoms which may be traced back to the sympathetic. These are v. Graefe's sign, widened lid slits (Stellwag's sign), diarrhea, exophthalmos, tachycardia, sweating. Yet the etiology for these, if this similarity of manifestations be adopted, may be ascribed to the activities of the thyroid hormone.

The influence of the thyroid upon carbohydrate metabolism has been discussed above. The alimentary glycosuria so frequently found in Basedow's disease may be explained either by an increased inhibition of the action of the pancreas by thyreoido-globulin or, what is more probable in view of the adrenalemia, by an increased adrenalin action.

As to the relation of diseases of the thyroid to other endocrinopathies, it may be noted that the changes of the blood—leucopenia or leucoanemia with absolute or relative mononucleosis, eosinophila and diminished coagulation time—are also found in other endocrinopathies when these are combined with status thymico-lymphaticus (Borchardt) since this is the principal cause of the blood changes. According to Wolfsohn, the same blood picture is characteristic of anaphylaxis, and in this condition vagotonia is demonstrable. In view of this, Wolfsohn thinks it not improbable that the thyreosis is an anaphylactic phenomenon. The foreign proteid in these cases would be an excess of some albumin containing iodine and secreted by the thyroid.

Cushman has recently tried to explain the causal relationship between Basedow and vago and sympathicotonia by assuming an intermittent form of Basedow (without struma) which is associated with other severe vegetative symptoms as paroxysms of bronchial asthma and tabetic-like abdominal crises due to high blood pressure. The Basedow symptoms in tabes, in this way, may be regarded as disturbance equivalent to vegetative system symptoms, *i. e.*, as a symptomatic Basedow with tabes as the basis, causing tabetic affections of the vegetative nervous system (Malaisé), which causes thyreotoxic symptoms.

The theory of Gottlieb, that thyreotoxin sensitizes both parts of the vegetative nervous system for the action of adrenalin, is of value in connection with the vago-sympathetic form of Basedow's disease which, as we have seen above, is often complicated by psychic symptoms.

(*f*) A gland of internal secretion, whose influence upon the vegetative system has been discovered in the last few years, deserves mention in closing. This gland is the paired parathyroid or glandulæ parathyroidæ. In the course of our discussion we have mentioned this gland not only in the general part in speaking of pharmacological matters and of the influence of endocrinous glands upon the mind, but also in the special part in speaking of metabolic anomalies and vegetative neuroses resultant upon some disturbance of the endocrinous glandular equilibrium.

It is well known through both clinical observation in thyreoplasia and experimental researches upon parathyroidectomized animals, that the absence of the parathyroids and the accessory parathyroids is responsible for tetany in its most various classical and abortive forms. These are tetany in children, in workmen, in gastric disease, in acute infections, during various intoxications, in pregnant

women, during parturition and in post-partem cases, in nervous diseases, after operations in the cervical region, etc. The pathologico-anatomic basis of all of these forms of tetany is supposed to be an organic or functional disturbance of the normal activity of the parathyroid glands.

Of the various theories concerning the function of the parathyroids (Pineles, Chvostek, Pfeiffer and Mayer, Eppinger, Falta and Rudinger) that of Falta and Rudinger is, in my opinion, the best. This theory is that the parathyroids have a very definite relationship to the vegetative nervous system.

The precise experiments of Falta and Kahn have shown us the following in relation to this most interesting of questions. The symptoms of tetany result in the main from a state of over-irritability or over-irritation of the nervous system in its motor, sensory and vegetative parts.

The over-irritability of the vegetative nerves, particularly noticeable in the acute stages of tetany, is not only mechanical but, as experiments with adrenalin and pilocarpin have shown, also chemical. The end organs of the vegetative nerves are the site of many symptoms of over-irritation (Ibrahim, Falta)—pylorospasm, spasm of the internal sphincters of the bladder and intestines, angiospasm, spasm of the ciliary muscles, disturbances in the heat-regulating system, increased cardiac action, angiospastic edema, transient leucocytosis, hypersecretion of various glands, sweat, salivary, lachrymal, gastric and intestinal, and so forth.

All the manifestations and disturbances of intermediary protein metabolism are assumed to be due to increased irritability of the ganglion cells of the spinal cord, from which both the somatic and vegetative neuroses arise. It is chiefly the peripheral neurones which are in a state of over-irritability, but higher neurones as well may be found in this condition.[5]

According to the same authors, the parathyroids normally act as a depressant upon the irritability of the ganglion cells, perhaps by increasing the intracellular calcium assimilation in the central nervous system. When the parathyroids are unable to cope with normal or increased demands on the part of the body, a state of over-irritability of the nervous system develops.

That it is not nerve or reflex paths primarily which cause tetany, but adrenalin substance from the parathyroids, is shown by the fact that a parathyroid gland free of nerve and blood supply which has

[5] See chapter on Tetany in Jelliffe and White, Diseases of the Nervous System, 2d ed., 1917, for a more searching analysis of this situation.

been successfully transplanted between the abdominal fascia and musculature will serve the function of a normally placed parathyroid and will prevent tetany.

Georgopulos maintains that it has not been proven that the parathyroids exert an inhibitory action upon the secretory action of the chromaffin tissues, but, in the light of the work already done, supposes that action is limited to an inhibition of the action of the secretion of the chromaffin system.

It is very hard at the present time to say whether myoclonia, myasthenia, and myotonia are, as Lundborg claims, due to a disturbed functioning of the parathyroids. As little settled is Chvostek's theory of the antagonistic relations of tetany and myasthenia to the parathyroid glands and the vegetative system. According to this theory tetany with its spasms, increased irritability and psychic irritability, is due to parathyroid hypofunction, while myasthenia with its fatigue, diminished irritability and psychic depression is due to parathyroid hyperfunction. The antagonistic and stimulating actions of the parathyroids are, however, not yet clearly understood. The subject is by no means a closed one, and the complete elucidation of this complicated matter is coupled with many almost insuperable difficulties which in being overcome will, without doubt, cost experimenters not only great trouble but much time.

(*g*) The sex glands and the hypophysis are placed side by side in the scheme of metabolism worked out by the school of van Noorden. The recent investigations of Aschner have demonstrated a singular dissociation. As far as the links in the chain of endocrinous glands can be worked out, it seems that the hypophysis and sex glands are synergistic in their influence upon fat and protein metabolism, antagonistic in their influence upon calcium and carbohydrate metabolism. It is well known that they have much to do with the form of the body in general and with skeletal growth and secondary sexual characteristics in particular. Less certain is the question discussed on a former page of the relation of the hypophysis and the nearby vegetative trophic centers lying in the midbrain hypothalamus to the trophic changes and disturbances of metabolism of youthful and more particularly of adult individuals.

The libidogenous hormone comes most probably, but not certainly, from the testicle which, besides the spermatogenic cells, contains the interstitial cells of Leydig. It is these latter, in all probability, and not the spermatogenic cells which furnish the libidogenous hormone. Both the size and the number of these Leydig cells diminish after castration and in old age. On the other

hand, the selective action of the X-ray destroys the spermatogenic elements, but leaves the libido intact.

I shall not discuss at any greater length these interrelationships which seem to have so little to do with our subject, the vegetative nervous system. They are but meant to recall the long recognized fact that, as Munzer has said, we are not in a position to say that any endocrinopathy, particularly of the hypophysis and sex glands, has its cause in one single pathological alteration of some particular endocrinous gland.

We shall not touch at all upon the hormones of the thymus and epiphysis, glands having an antagonistic action upon the chromaffin tissues, nor upon their relations to the vegetative nervous system. We must be entirely aware of the truth of Köhler's observation upon the difficulties which attend a separation of fact from theory in this relatively young and modern yet well-developed subject of hormonology.

In the growth of the significance of this subject, we must beware lest the endless profusion of details which experiments yield on all sides should not lead us in our zeal to draw conclusions from what is still purely hypothetical, and to believe things clear which can not yet be clearly made out in the gray distance of theory.

This youthful and hopeful branch of medical knowledge, vegetative or visceral neurology, undoubtedly deserves a prominent place in physiology as well as in the Clinic. The neurologist must also regard it his duty to include these subjects within his domain.

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INDEX

Addison's disease, 66
Adrenalin, 55
  mydriasis, 81
Angina pectoris, 114
Anemia, 112
Antagonism, 30, 71
Aortic plexus, 5
Argyll Robertson, 77
Aschner, 104
Asthma, 103
Autonomic, 34
Autonomy, 22

Babinski Nageotte, 80
Biotonus, 50
Bladder, 94, 98
Blood vessels, 28, 108

Carotid plexus, 5
Centers in spinal axis, 10
Cerebral stimuli, 29
Cervical sympathetic, 84
  vagus, 84
Cholin, 55
Chorda tympani, 19
Chromaffine, 70
Chromaffin ganglia, 70
Cocaine, 58
Colic, 93
Colon, 93
Communicating Tracts, 7
Comparative, 1
Cortical influence, 46

Dejerine Klumpke, 80
Double innervation, 33
Dribbling, 102
Dyspragia, 113

Electrical stimulation, 33
Embryology, 13
Embryonic metameres, 10
Emotions, 49
Endocrine glands, 20
  relations, 68
End organs, 32
Ephedrin, 55
Erection, 101
Erythromelalgia, 114
Esophagus, 87
Eye, 73

Facial, 19
Fibers, types of, 32

Ganglia, 4
  functions of, 28
Ganglion cells, 29
Gastro-intestinal, 87
Genitals, 94
Gooseflesh, 123
Grave's Disease, 65

Head zones, 43
Heart, 104
Higher centers, 35
Hippus, 81
Histology, 15
Hormones, 52
Horner, 79, 85
Hyperemia, 112
Hypophysin, 55, 86
Hypothalamus, 36
Hypophysis, 133

Infection, iii
Intermittent claudication, 113
Intestinal innervation, 91
  pain, 93
  sensation, 4
Intestine, large, 91
Intoxication, iii
Introduction, ii
Iodothyrine, 55

Kidney, 128

Lacrimal glands, 81
  nuclei, 18
Laryngeal plexus, 5
Lateral cell column, 17
Local vagotonia, 63
Loewi, 81

Mammals, 2
Median cell column, 17
Metabolism, 126
Metameric system, 1
Microscopical anatomy, 4
Morphine. 54
Motor reflex, 43
Mydriasis, 81
Myoneural junction, 24
Myxedema, 65

Neopallium, 2
Neuroses, 69

Oculomotor, 19

Organic neuroses, 69
Organ reflex, 43
Orgasm, 100, 102
Otic, 19

Pain, 43, 45
  intestine, 93
Pancreas, 128
Parathyroid, 131
Pathology, 62
Pharmacology, 52
Physiology, 22
Pilocarpin, 56
Pilomotor, 122
Pituitrin, 56
Plexuses, 5
Preganglionic fibers, 23
Priapism, 101
Prostatorrhea, 102
Psychic trauma, 67, 68
Psychogalvanic, 49
Pupillary changes, 78
  nuclei, 18
Pupils, 74, 75, 76

Rami communicantes, 9
Raynaud's, 114
Rectum, 94, 95
Reflex, 25, 43
  arcs, 25
Reptiles, 2
Respiratory tract, 103
Rumination, 89

Secretion, 94
Salivary glands, 82
  nuclei, 18
Sensation and reflex, 23
Sensory and vegetative system, 27
  innervation, 26
Sex glands, 133
  organs, 120
Sheathed fibers, 27
Skin, 122
Sleep, 71
Smooth muscle, 23
Somatoneuroses, 70
Spermatorrhea, 102
Spinal connections, 5
Stimuli, 29
Stomach, 87
Summated Reflexes, 26
Sympathicotonia, 61
Synapses, 6, 8, 24
Sweat, 119

Tabetic crisis, 41
Tenesmus, 102
Thoracic plexus, 5
Thyroid, 64, 65, 129
Tympanic, 19

Unsheathed fibers, 27
Urhirn, 1
Urogenital, 94
Uterus, 102

Vagotonia, 61
  genesis of, 64
Vagotonic, 53, 55
Vagus, 85
  nuclei, 18
Vascular tone, 112
Vasomotor, 111, 113
Vegetative organs, ii
  reflex, 25, 42
Visceral neurology, iii
  pathology, 70
Vomiting, 89

White rami, 6

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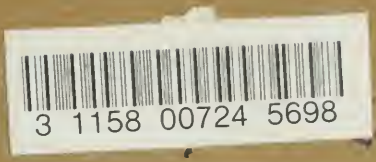
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