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PERIPHERAL OR LOCAL REFLEXES

by

M. V. Sergiyevskiy

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Kuybyshevskiy Meditsinskiy Institut

M. V. SERGIYEVSKIY

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ABSTRACT: There has been a substantial amount of research on the physiological and pathological interactions of the various elements of the alimentary tract and the interrelationship of its motor, secretory, and excretory functions. There have also been investigations of the reflex interactions among the organs of the urogenital system and of the influence of interoceptive stimulation on the circulatory system, endocrine glands, skeletal musculature, etc. There has also been a rather large amount of research intended to determine where in the central nervous system various interoceptive reflexes are completed. However, in comparison with the numerous and diverse investigations of central interoceptive-reflex mechanisms, the work done on the possibility of completion of reflex arcs in the peripheral autonomic ganglia has been totally inadequate. This monograph intentionally devotes a great deal of space to describing certain structural characteristics of the centripetal intervertebral neurons, principally the polyvalency of their endings. This is necessary in order to gain a clear idea of the possibility of formation of peripheral reflex arcs through linkage of the intervertebral centripetal neurons and the centrifugal neurons of the peripheral sympathetic ganglia. Where the author presents experimental data obtained in his laboratory he does not describe the respiratory reaction, the blood-pressure reactions in the common carotid artery, or the muscular reactions to adequate interoceptive stimulation seen in his observations. These reactions have been repeatedly investigated and are well known; their mechanism has been studied with sufficient thoroughness. In the experimental

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part of the book he dwells on those reactions of the internal organs observed in the presence of changes in blood pressure in isolated arteries and abdominal organs and in the absence of general respiratory, circulatory, and muscular reactions. Sufficient attention has not been paid to determination of the mechanism of such reactions. This monograph thus presents data from the literature and experimental data that give us grounds for asserting that vertebrates, including the higher vertebrates, have peripheral, or local reflexes, which form a component of the unified neurohumoral regulatory system and manifest their activity under both normal and pathological conditions. The concluding chapter of the book describes the structure of peripheral reflex arcs and analyzes the characteristics of their reflex activity.

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INTRODUCTION

In all animals, from the invertebrates to the higher mammals and man, there are numerous neural ganglia and plexi in the body cavities and internal organs. However, the physiological significance of these structures is still unclear.

The autonomic nervous system of arthropods contains sensory fibers whose somae form autonomic ganglia (A.A. Zavarzin). According to the data of a number of researchers, these ganglia exhibit reflex activity in invertebrates (Ye.I. Sinel'nikov and T.P. Gugel'-Morozova, 1937; et al.).

Is this property retained in the autonomic ganglia, particularly the sympathetic ganglia, of vertebrates? If it does persist, to what extent can these ganglia participate in reflex regulation of the vital activity of the internal organs? In higher animals do the sympathetic ganglia serve exclusively as conductors for centrifugal impulses and is neural regulation of vital activity effected solely by the central nervous system?

Proper resolution of these problems is of theoretical and practical importance, but the existing physiological and clinical literature gives contradictory answers. One of the principal characteristics of the evolution of animals is the development of "central stations," the analyzers of the cerebral cortex.

In this connection I.P. Pavlov wrote: "I feel that the main center of nervous activity lies in the perceptive portion of the central stations, this forming the basis for the development of the central nervous system, which is due to the brain, principally the cerebrum ... The centrifugal portion of these stations is purely effector in character, as can readily be imagined: the same muscles can be used for thousands of purposes, as dictated by the activity of the perceptual apparatus, which determines the combinations formed by the cells of given nerves."*

There is a question as to whether the reflex arcs formed in the peripheral ganglia of invertebrates have disappeared as a result of the evolutionary development of a higher form of regulation. Here we are speaking of elimination of the perceptual portion of the peripheral ganglia. This could have occurred if the reflex activity of these ganglia was an obstacle to the functioning of higher forms of reflex regulation, perhaps when the peripheral reflex apparatuses continued to function independently of the central nervous system. The spinal cord contains reflex centers, but they do not function autonomically, operating as constituents of the reflex mechanisms of the brain. It can be hypothesized that the same is true of the reflex activity of the peripheral ganglia.

There is no question that the internal organs of higher animals do not function autonomically, independently of general existential conditions and the general regulatory activity of the cerebral cortex. The cortex is the highest regulator of vital activity in the higher animals and man. The special evolutionary development of the brain, including the perceptual "central stations" of the cortex, does not necessarily entail elimination of the reflex activity of the peripheral ganglia, particularly since this activity is no impediment to the development and functioning of higher forms of regulation.

Peripheral, or local reflexes were discussed by I.M. Sechenov (1866), I,P. Pavlov, and a number of other noted researchers. In his

30th lecture I.P. Pavlov said: "The act of defecation is reflexive ... and the first instants in which centripetal stimuli are converted to centrifugal stimuli occurs in some ganglion outside the central nervous system."* However, despite such authoritative assertions of the possibility that peripheral reflexes may exist, they have been denied by a quite substantial number of researchers (Langley, 1893, 1925; L.A. Orbeli, 1928; et al.). The concept represented by the term "peripheral, or local" reflex completely replaced that designated by the term "axon reflex." After the investigations of Langley and Anderson (1893) many authors did not distinguish between the axon reflexes of sensory and centrifugal nerve fibers; attempts were made to attribute all the data indicating the existence of peripheral reflexes to axon-reflex activity on the part of centrifugal sympathetic fibers. Even N.M. Sokovnin, one of the first to present experimental verification of "peripheral" reflexes (1877), was among the founders of the theory of axon reflexes in centrifugal sympathetic fibers.

We became interested in problems of peripheral neural regulation in the nineteen-twenties, in connection with our study of the physiology of the prostate gland. During the nineteen-thirties, as a result of our investigations of the physiology of circulation, we amassed more and more data that cast doubt on the validity of the theory of axon-reflex transmission along the centrifugal sympathetic fibers under natural conditions.

Our laboratory began a systematic study of the problem of peripheral, or local reflexes and axon reflexes in the centrifugal sympathetic fibers in 1939. Our concepts of the mechanisms of peripheral nervous regulation have undergone many changes between 1950 and the present. The concept of "peripheral, or local reflexes" has gained ever greater currency and acceptance. The number of researchers studying this problem has increased. In particular, at the 1957 Conference of Anatomists, Histologists, Embryologists and Topographical Anatomists in Minsk I.A. Bul'gin reported on the existence of so-called true sympathetic afferent fibers, N.P. Ivanov discussed the many intragangliar interneuronal pathways in the heart, and S.G. Kul'kin reported on the many interneuronal pathways in the wall of the urinary bladder. In 1957 Ye.K. Sepp advanced the hypothesis that Dogel' cells of the first type are not the second element in the vagus system. Dogel' cells of the first and second type form reflex arcs, the vagus nerve regulating the excitability of cells of the first type and of the local reflex arcs.

V.V. Zakusov and O.V. Ul'yanova (1957) feel that various drugs influence local viscerovisceral reflexes, acting on the autonomic ganglia. M.R. Mogendovich (1957) attempted a very brief survey of the literature dealing with peripheral and axon reflexes.

The recent histological research conducted by N.G. Kolosov and his colleagues has been of great value in establishing the existence of peripheral, or local reflexes. Since we were in constant contact with his work we were able to make use of his observations and theoretical conclusions. It was obvious that the histological investigations of N.G. Kolosov, I.F. Ivanov, G.A. Koblov, and others and our physiological investigations supplemented one another; this became especially clear at the Conference on Interneuronal Linkages organized by the Institute of Physiology imeni I.P. Pavlov of the Academy of Sciences USSR in 1955. The published results of the research carried out by N.G. Kolosov and his colleagues lead us to conclude that there are contacts between the centripetal and centrifugal sympathetic neurons in the peripheral ganglia. The need for a comparison of the physiological, clinical, and histological data on peripheral and axon reflexes is now obvious.

The initial difficulties and failures in studying the sensitivity of the internal organs resulted both from deficiencies in the observational technique and from incorrect theoretical premises; attempts were made to draw an analogy between this sensitivity and that which obtains on stimulation of the sense organs during perception of changes in the environment, i.e., the necessary development of a definite sensation. However, the internal organs may not develop such definite sensations and reactions on stimulation and, for a long time, this served as grounds for denying that they possessed sensitivity. One of the difficulties encountered in resolving this problem was the lack of clarity in the theories of many researchers who have studied the mechanisms by which the unity of organism and environment is regulated. Those investigators who explained their data on the basis of theoretical concepts of the internal unity of organism and environment made the greatest contributions to the development of the theory of the sensitivity of the internal organs.

Of great importance were the investigations and theoretical generalizations of I.M. Sechenov (1866), who used his observations of the reactions of animals to mechanical and electrical stimulation of the mesenteric nerves as grounds for concluding that they felt pain. As we know, humans feel pain when the activity of the alimentary tract is disrupted in various ways. Some reflexes originating in the internal organs can be perceived, while others cannot. Sensory signals from all the internal organs create a general background of sensation, a gross feeling, which takes the form of the so-called sense of general well-being in healthy and of general malaise in the sick. This background is variable and such sensations as hunger, thirst, fatigue, malaise, pain, sexual desire, and so forth, can be isolated from it.

Various clinical investigations that established that the activity of one internal organ depends on organic or functional disruptions served as a great stimulus to experimental observation of reflexes originating in the internal organs. Thus, there are disruptions of cardiac activity in primary diseases of the stomach, liver, gall bladder, etc.; substantial changes in gastric activity develop in primary diseases of the liver and appendix; pain in definite areas of the body surface and changes in the tonus of individual groups of striated muscles are generally noted in diseases of the heart and various elements of the alimentary tract, as was pointed out by S.P. Botkin (1875). The complex of observations on the physiology and pathology of the cardiovascular and alimentary systems and in the field of higher nervous activity under the supervision of I.P. Pavlov were of great value in the development of the theory of the sensitivity of the internal organs.

The principle of a bilateral linkage between the internal organs and the central nervous system was fruitfully used by Hering and Brewer (1868) to develop a theory explaining the reflex autoregulation of respiration. The same principle of a two-way relationship between the peripheral organs and the central nervous system runs like a thread through all the work of I.P. Pavlov's students. It is the basis for the famous theory of the reflex autoregulation of organs and systems. In this connection, Pavlov wrote: "... the afferent nerves running from the heart influence cardiac activity. This is quite understandable, since it is very important that the heart be able to induce certain effects and to regulate itself."* I.P. Pavlov's work on the physiology and pathology of digestion yielded new, exceptionally significant data indicating that the entire digestive apparatus functions as a unit because of its two-way neural linkage to the central nervous system: the activity of any segment of this apparatus can be reflexively actuated and altered by signals from its other elements. The interrelationship of the activity of different segments of the alimentary tract was subsequently studied in various investigations at numerous laboratories and by I.P. Pavlov's students A.F. Samoylov, K.M. Bykov, and A.D. Speranskiy. A.F. Samoylov (1930) cited a number of clear examples of the physiological importance of this two-way linkage in the formation of "annular excitation rhythms'; this phenomenon was subsequently confirmed by the investigations of Heymans (1929) and Koch (1931), who studied the autoregulation of various functional systems. However, Heymans and Koch believe that the neurohumoral mechanisms underlying respiratory regulation exist independently and that annular excitation rhythms are transient rather than constant factors.

The physiological importance of an annular excitation rhythm was pointed out in our previous works (1947, 1950, 1955). The complex of stimuli consisting of contraction of the respiratory muscles, movement of the chest, and changes in the partial carbon dioxide and oxygen pressures and pH causes excitation of the centripetal nerve endings of the respiratory apparatus and vascular system and formation of inspiratory and expiratory impulses; this in turn causes an interdependent alternation of inhalation and exhalation – respiratory autoregulation. An annular excitation rhythm is a constant-action factor in respiratory regulation.

K.M. Bykov and his students (V.N. Chernigovskiy, A.V. Rikkl', E.Sh. Arapet'yants, et al.) greatly advanced the theory of the physiological significance of two-way innervation. Their research left no doubt that the internal organs, which have a two-way linkage to the central nervous system and are constantly regulated by it during vital activity, themselves dispatch informative signals regarding their condition to this system and influence its functional state. As a result, the internal organs can reflexively modify their own functional state, the vital activity of other organs, and the general vital activity of the organism.

Investigations of this type are of great importance: they extend and supplement I.P. Pavlov's conclusions regarding the sensitivity of various segments of the vascular system. They have also refuted the erroneous conclusion of Heymans and other researchers that receptors have a rather limited distribution in the vascular system, being localized only in the cardioaortic region, the carotid sinus, the carotid gland, the pulmonary vessels, and the ostia of the venae cavae.

Also to the credit of K.M. Bykov and his students is the fact that they extended and intensified research on the centripetal innervation of the internal organs, which began during the 19th and early 20th centuries. Despite the large amount of data amassed, the study of this problem had a fragmented character as a result of a lack of systematization and purposiveness (Goltz, 1863; Mayer and Pribram, 1872; N.P. Simanovskiy, 1881; et al.).

There has now arisen the quite distinct notion that the entire vascular system and each internal organ have centripetal nerve endings sensitive to various stimuli (mechanical, thermal, chemical, electrical, or physicochemical). The receptor system, varying in stimulus specificity, also differs in distribution, being both diffuse and concentrated into fields; this is undoubtedly of great importance in determining the sensitivity of different regions of the vascular system and of different organs.

In studying reception in the vascular system and internal organs, attention was at first concentrated on blood-pressure and respiratory reactions, which are essentially indicators of interoceptive reactions. It is not surprising that an enormous amount of data was amassed on the characteristics of the respiratory and blood-pressure reactions to stimulation of the internal organs and vascular system. Experimental investigations of this type serve as a basis for interpreting the numerous clinical observations of various types of cardiovascular disturbances in diseases of the internal organs; their importance cannot be underestimated. Cardiovascular activity can in turn induce reations in the internal organs, both through changes in their blood supply and through reflex influences. The cardiovascular system is an extensive receptor field whose excitation or inhibition can reflexively modify the activity of any organ. The various reflexive influences of the carotid sinuses and glands on different organs and functional systems have been studied in greatest detail.

Heymans (1955) made a thorough review of the literature on the receptors of the carotid glands, Dawes and Comroe (1954) reviewed that on the chemoreceptors of the heart and lungs, Ya. Ryzhevskiy (1957) that on the interoceptors of the internal organs, O.P. Minut-Sorokhtina and B.Z. Sirotin (1957) that on the receptors of the veins, M.R. Mogendovich (1957) that on reflex interactions between the locomotor and visceral systems, V.N. Chernigovskiy (1960) that on the interoceptors, etc.

There has been a substantial amount of research on the physiological and pathological interactions of the various elements of the alimentary tract and the interrelationship of its motor, secretory, and excretory functions, a study begun by I.P. Pavlov. A number of fundamental theoretical works have been published on this topic, the most important of which are those by K.M. Bykov (1941), I.P. Razenkov (1948), A.V. Solov'yev (1953), B.P. Babkin (1960), K.M. Bykov and I.T. Kurtsin (1960), and R.O. Faytel'berg (1960). There have also been investigations of the reflex interactions among the organs of the urogenital system and of the influence of interoceptive stimulation on the circulatory system, endocrine glands, skeletal musculature, etc. There has also been a rather large amount of research intended to determine where in the central nervous system various interoceptive reflexes are completed. However, in comparison with the numerous and diverse investigations of central interoceptive-reflex mechanisms, the work done on the possibility of completion of reflex arcs in the peripheral autonomic ganglia has been totally inadequate.

In this monograph we will intentionally devote a great deal of space to describing certain structural characteristics of the centripetal intervertebral neurons, principally the polyvalency of their endings. This is necessary in order to gain a clear idea of the possibility of formation of peripheral reflex arcs through linkage of the intervertebral centripetal neurons and the centrifugal neurons of the peripheral sympathetic ganglia. In that part of the book where we present the experimental data obtained by our laboratory we will not describe the respiratory reaction, the blood-pressure reactions in the common carotid artery, or the muscular reactions to adequate interoceptive stimulation seen in our observations. These reactions have been repeatedly investigated and are well known; their mechanism has been studied with sufficient thoroughness. In the experimental part of the book we will dwell on those reactions of the internal organs observed in the presence of changes in blood pressure in isolated arteries and abdominal organs and in the absence of general respiratory, circulatory, and muscular reactions. Sufficient attention has not been paid to determination of the mechanism of such reactions.

This monograph thus presents data from the literature and experimental data that give us grounds for asserting that vertebrates, including the higher vertebrates, have peripheral, or local reflexes, which form a component of the unified neurohumoral regulatory system and manifest their activity under both normal and pathological conditions.

The concluding chapter of the book describes the structure of peripheral reflex arcs and analyzes the characteristics of their reflex activity.

Manuscript Page No.	[Footnotes]
2	I.P. Pavlov. Dvadtsatiletniy opyt ob'yektivnogo izucheniya (vysshey) nervnoy deyatel'nosti (povedeniya) zhivotnykh [Twenty Years' Experience in Objective Study of (Higher) Nervous Activity (Behavior) of Animals], Leningrad, 1938, page 154.
3	I.P. Pavlov. Lektsin po fiziologii. 30-ya lektsiya [Lectures on Physiology. 30th Lecture]. Leningrad, 1952, pages 217-218.
6	I.P. Pavlov. Lektsii po fiziologii.Moscow-Leningrad, 1952.

Chapter 1

BASIC HISTOLOGICAL DATA ON SENSORY-NERVE ENDINGS IN THE INTERNAL ORGANS AND THE POSSIBILITY OF REFLEX-ARC COMPLETION IN THE PERIPHERAL GANGLIA

The urgency of histological research on the sensory innervation of various organs and the substantial interest of physiologists in such research can be seen from I.P. Pavlov's remark on A.S. Dogel's report (1897) "O nalichii okonchaniy chuvstvitel'nykh nervov v serdtse i krovenosnykh sosudakh" [The Presence of Sensory-Nerve Endings in the Heart and Blood Vessels]: "Physiologists will hear of the discovery of sensory nerves in the heart with understandable joy, since this discovery lays bare a subject of discussion and hypothesis. That which physiologists only surmised has now been made visible."*

The noted Soviet neurohistologist B.I. Lavrent'yev (1948) later wrote: "... by the turn of the 20th century histologists had described sensory-nerve endings in many organs, including the heart, the blood vessels, the smooth musculature of the urinary tract, and the ciliary muscle. Russian histologists (Arnshteyn, Dogel', Timofeyev, Smirnov, Agababov, Gerberg, Ploshko, et al.) made particularly great contributions in this area ... however, the lack of physiological data caused many important morphological observations to be undervalued and then completely forgotten."

These investigations were continued in the noteworthy work of Soviet morphologists (A.N. Milavskiy, B.I. Lavrent'yev, N.G. Kolosov, G.F. Ivanov, I.F. Ivanov, B.A. Dolgo-Saburov, and S.M. Milenkov).

The successful continuation of research on the morphology of the nervous system was considerably stimulated by advances in the modern physiological study of mechanisms of functional regulation, particularly of interoception.

Detailed studies have been made of the sensory innervation of the heart (A.Ye. Smirnov, 1895; B.I. Lavrent'yev, 1948; Ye.K. Plechkova, 1948; D.N. Vyropayev, 1948; A.Ya. Khabarova, 1949, 1958, 1961), various segments of the vascular system (T.A. Grigor'yeva, 1949, 1954; N.G. Smirnova, 1948; G.F. Ivanov, 1945; L.I. Falin, 1948; V.M. Godinov, 1949; B.A. Dolgo-Saburov, 1948, 1949, 1958; G.F. Mal'kov, 1949; G.I. Zabusov, 1944; A.P. Maslov, 1950, 1958, et al.), the alimentary tract (A.S. Al'tshul, 1940, 1948; N.G. Kolosov and A.M. Moscheryakov, 1938; N.G. Kolosov, 1935; I.I. Kolesnichenko, 1943; N.P. Prosfirova, 1949; S.M. Milenkov, 1950; et al.), the lymph nodes (T.A. Odynets, 1957), the urogenital organs (B.I. Lavrent'yev, 1943; Ye.K. Plechkova, 1948; I.G. Fel'dman, 1935; et al.), the endocrine glands (V.I. Il'ina, 1948; et al.), the solar plexis (S.M. Milenkov, 1950; G.A. Kablov, 1950, 1956, 1957; et al.), the respiratory passages (V.F. Lashkov, 1948, 1961; M.T. Mogila, 1948, et al.), and the lungs (G.I. Zabusov, 1944; V.V. Kupriyanov, 1953; V.M. Sklyandeva, 1957; V.F. Lashkov, 1961; et al.).

In considering the general regularities of receptor structure, B.I. Lavrent'yev (1948) feels it expedient to distinguish free and enclosed nerve endings when classifying receptors. Encapsulated nerve endings are a special case of the latter group. The two basic groups of receptors differ in structure and function. Free nerve endings vary in appearance, but are characterized by the fact that they lie free among the surrounding cells, not forming noticeable morphological links to them. Regardless of their form, enclosed nerve endings are characterized by links between their axis cylinders and adjoining cells. The special cells to which the enclosed nerve endings of many receptors are joined are derivatives of Schwann cells and the process that takes place in them may be similar to the excitation of nerve tissue: "... be that as it may, a special cell must be regarded as a structure that transforms the stimulus applied to the nerve ending" (B.I. Lavrent'yev, 1948). This conclusion of Lavrent'yev's merits special attention, since it opens up new prospects for resolving the question of possible links between sensory innervation and the surrounding tissue.

Using functional characteristics as a basis, B.I. Lavrent'yev distinguished mechanoreceptors, muscle receptors and chemoreceptors. Mechanoreceptors signal extension of the tissue in which they ramify and are very widely distributed. The sclera, the cartilaginous portion of the diaphragm, the pia mater, the cardiovascular system, all components of the alimentary tract, the urinary bladder, and other organs are rich in these receptors. They are characterized by the fact that they follow the fibers of the tissue (e.g., the connective-tissue fibers of the sclera and the cartilaginous center of the diaphragm) or twine about it (e.g., the blood vessels). In either case slight tension should cause impulses to develop in the receptors.

Muscle receptors, which have been studied in detail in smooth muscle, have a rather uniform structure and consist of myelinated nerve fibers, whose fine branches run between the muscle fibers and terminate in enlargements or loops. They signal contraction of the muscle tissue.

Chemoreceptors must contain special cells and their structure has much in common with that of the receptors of the gustatory organ. These cells lie against the walls of the blood vessels and are obviously stimulated by the chemical substances traveling through the vessels. The excitation produced is then transmitted to the nerve endings (B.I. Lavrent'yev, 1948). The current literature on this problem has been discussed in sufficient detail in the books by B.A. Dolgo-Saburov (1958), N.G. Kolosov (1952, 1954), T.A. Grigor'yeva (1954), V.V. Portugalov (1955), and Yu.M. Zhabotinskiy (1953). It can be assumed that receptors of this type have the ability to secrete active substances into the underlying tissue when excited.

Histological investigations of the innervation of different tissues by the same sensory nerve fiber merit special attention. This phenomenon has come to be called polyvalent innervation. Many authors (A.S. Dogel', 1898; D.A. Timofeyev, 1895; A.Ye. Smirnov, 1895; A. Morrison, 1898, 1899) noted branching of sensory fibers innervating striated muscles and superficial tissues. This phenomenon was first established for the internal organs in the laboratory headed by B.I. Lavrent'yev, by A.S. Al'tshul (1940), who demonstrated that in the cat the same sensory nerve fiber ramifies to terminate in the smooth muscle of the intestine, in a blood vessel, and in the vicinity of the ganglia of Auerbach's plexis. The same pattern was shown by Ye.K. Plechkova (1948) for the ramified nerve fibers in the myocardium and cardiac blood vessels.

In B.I. Lavrent'yev's opinion, the ramification of sensory fibers in autonomic ganglia makes it possible to signal the central nervous system regarding the passage of impulses from preganglionic to postganglionic fibers in the sympathetic nervous system. As a result, the transmission of excitation in the ganglia of the autonomic nervous system is under the constant control of the central nervous system. In this connection B.I. Lavrent'yev (1948) poses a very important question: "If the neurofibrils of the spinal sensory tracts participate in intracellular communications and even extend to the pericellular apparatus, would not stimulation of sensory fibers produce motor effects in the autonomic nervous system." Lavrent'yev notes that if this is so the results of Ken-Kure's experiments (stimulation of the posterior roots causes motor and secretory effects in the internal organs) and the irradiation of heart pains in angina pectoris are due to precisely these characteristics of sensory-fiber endings. Nevertheless, Lavrent'yev concludes: "The arguments presented here are still hypothetical. Further work in this area is necessary to verify them." Unfortunately, Lavrent'yev did not subsequently conduct such work.

A.S. Dogel' (1897) and S.Ye. Mikhaylov (1909) gave the first indications of the presence of sensory endings in the ganglia of the autonomic nervous system. S.Ye. Mikhaylov described six types of sensory endings in the solar plexus and the ganglia of the sympathetic trunk: 1) end-plates, in which almost all unmyelinated nerve fibers terminate; 2) dendritic endings, in which myelinated fibers terminate in connective-tissue filaments between groups of nerve cells; 3) unencapsulated end-brushes, which are also found in intercellular connective tissue; 4) reticular endings; 5) end-brushes with plate- and club-like structures; 6) end-bulbs.

In citing Mikhaylov's data, G.A. Kablov notes that he was able to detect new forms of receptors in the solar plexus, these lying between nerve cells, in bundles of connective tissue, in the glia, between bundles of nerve fibers, and in the gangliar capsule. Koblov points out that, if all the neural structures described by Mikhaylov and observed in our preparations are regarded as sensory, we have discovered the principal groups of sensory structures found in nerve cells, trunks, and tracts.

In S.M. Milenkov's opinion (1950), the receptor apparatus of the solar plexus of an individual who died of a dystropic disease lay in the connective-tissue layers between the gangliar nerve cells and consisted of a thick myelinated fiber covered with a thin, amorphous connective-tissue membrane that passed into an end-bulb. The receptor bulb was located on a venule of considerable size.

The receptor bulb was in such close contact with the venule that the latter was greatly compressed at the contact site, its lumen being smaller by a factor of two than in other areas. Milenkov notes that receptor location exhibits similar characteristics in other organs, including the spleen. The slightest increase in venous pressure is quickly transmitted to the receptor bulb. It can be assumed that such receptors serve primarily a baroreceptive function.

The structural variability of encapsulated receptors, according to Milenkov, forces us to surmise that they serve other functions (chemoreception, osmoreception, nocioreception, etc.). The relative sparcity of encapsulated receptors along venules and capillaries gives us grounds for assuming that they perceive signals from an entire area or from the field surrounding them. S.M. Milenkov has described polyvalent innervation in the skin. Fibers run from the Meissner bodies in the epidermis to the granular layer. The Meissner bodies are angioceptors, while the fibers rising from them are touch and temperature receptors.

In addition to G.A. Kablov, other workers in the laboratory headed by N.G. Kolosov have found receptor apparatuses in ganglia of the autonomic nervous system; these include N.I. Lyapin (1951, 1953), who discovered such structures in the esophageal ganglia, S.M. Shindin (1958), who observed them in the ganglia of the pelvic plexus, and others.

N.I. Lyapin believes that ganglIar receptors are characteristically located among the gangliar cells and are often isolated from them. The dendrites of the nerve cells pass into brushes and the mesh formed by these structures frequently lies on the gangliar cells. The similarity between sensory endings and motor cells merits special attention, since it creates a definite impression that there may be contact between the endings of sensory fibers and gangliar cells.

The presence of polyvalent sensory innervation in the vicinity of the arteries, veins, and capillaries of the glans penis and clitoris was demonstrated by A.P. Maslov (1950).

While these areas have the character of receptor fields, receptor structures are sparsely distributed in the vicinity of the ascending arterial vessels.

A characteristic of all vascular receptors is the fact that they are located at places where the blood-channel volume varies. The same nerve fiber may give rise to several sensory endings and the same segment of a vessel may have receptors of different origins. The polyvalent receptors in the arteries and veins provide a direct link between the genital corpuscles in the connective tissue and the receptors in the vascular walls. Polyvalent receptors in capillaries are distinguished by the fact that there is a free ending in the connective tissue, while there is often only one nerve fiber in arteries and veins. The receptor structures in the human heart either are distributed uniformly or form rather large groups (receptor fields). In some layers and regions of the heart there may be two types of receptors: compact endings with special cells and diffuse endings. These two types of endings often overlap (A.Ya. Khabarova, 1961).

We cannot regard the question of the characteristics of the interactions between sensory endings and the cells of peripheral sympathetic ganglia as being conclusively resolved. G.A. Kablov (1950) was unable to make a definite decision on whether the sensory endings in the ganglia of the solar plexus are receptors that perceive stimuli coming from the nerve cells. According to his observations, the sensory endings in these ganglia are not in contact with the somae of the nerve cells, but merely lie in direct proximity to them. The distribution of receptor structures in the ganglia of the solar plexus is such that they envelop all the elements of the plexus except the neural somae.

In Kablov's opinion, it is consequently necessary to introduce certain corrections into B.I. Lavrent'yev's hypothesis regarding the possible character of the control exerted by the central nervous system over the transmission of neural impulses from preganglionic fibers to the neurons of peripheral ganglia.

Such control of impulse transmission would require a pericellular sensory apparatus on the second neuron; however, according to Lavrent'yev's data, this structure does not actually exist. There is a great deal of reason to suppose that the central nervous system controls synaptic transmission in the sympathetic nervous system through chemoreception, utilizing the variation in the concentration of substances formed during impulse transmission and perception: it is not the individual impulses that are controlled, but the effect of a whole group of impulses.

The disagreement here thus lies in different concepts of the manner in which reception is effected, this being due to the as yet inadequate study of this very important and pressing problem. It should also be noted that the polyvalent endings of a nerve fiber may differ in diameter. This permits us to assume that conduction of different impulses along the same fiber is possible. We are in complete agreement with G.A. Kablov that physiologists and pathologists do not pay sufficient attention to this possibility.

B.A. Dolgo-Saburov (1958) gives some data on attempts to classify receptors.

On the basis of the material presented above and our many years of research, we have come to the following basic conclusions.

1. The neural pathways from the internal organs are extremely nu-

merous and diverse. They provide a constant linkage between the central regulatory structures and the periphery and ensure that the organism is highly adaptable to varying environmental conditions.

2. The sympathetic ganglia contain endings of centripetal spinal fibers, which are connected in various ways to different elements of the ganglia, including the neural somae. This diversity of connections leads us to conclude that some form of reception is possible in the ganglia (probably in the presence of an intermediate substrate in the form of special cells); this should in some way ensure constant control of the vital activity of the sympathetic ganglia by the central nervous system.

3. Polyvalency of endings has developed in the spinal sensory ganglia, this serving as a solid basis for assuming axon-reflex activity in sensory neurons.

4. The admission of reception from the peripheral autonomic nerve cells, including the sympathetic ganglia, inevitably leads to recognition of the possibility of impulse transmission to these ganglia from the endings of the sensory fibers that ramify into them. This can be further justified by taking into account the polyvalency of sensory fibers and the possibility that they exhibit axon-reflex activity.

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12	I.P. Pavlov. Polnoye sobraniye sochineniy [Complete Collected Works], Vol. 1, 1946, page 279.

Chapter 2

PERIPHERAL, OR LOCAL REFLEXES AND AXON REFLEXES

The theory of peripheral, or local reflexes developed from the substantially earlier theory of axon reflexes. The hypothesis that reflex arcs may be completed in the peripheral sympathetic ganglia was repeatedly advanced by leading physiologists, morphologists, and representatives of various clinical medical disciplines, particularly Vulpian (1864), I.M. Sechenov (1866), Claude Bernard (1862, 1871), V.M. Bekhterev (1895), I.P. Pavlov, and others.

In this connection V.M. Bekhterev (1895) wrote: "The sympathetic nervous system is essentially an offshoot of the central nervous system ... and consists of a chain of neural elements, both motor and sensory, that make contact with and adjoin one another in various ways; these elements conduct impulses from our internal organs to the brain." Speaking of the mechanism of the rectal reflex, I.P. Pavlov noted: "the act of defecation is reflexive. The need to evacuate makes itself known through the sensory nerves located in the rectum. There are several centers through which this reflex is effected, lying in the lower intestine, the spinal cord, and even the brain ... this can be shown by clinical data, laboratory observations, and our own experience. We must first recognize the immediate intestinal centers, then the spinal centers, and finally the cerebral centers. The lower centers consist of ganglia in the abdominal cavity. That we must acknowledge the existence of these centers is demonstrated by the fact that, if we destroy the entire spinal cord of an animal from the first thoracic or even cervi-

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cal segments on, the evacuatory mechanism is at first completely disrupted but then gradually returns to normal. There is obviously a control apparatus for the sphincters and it must be assumed to lie in the lower abdominal centers ... the first case of conversion of centripetal stimuli to centrifugal stimuli thus occurs in some ganglion outside the central nervous system."*

However, I.M. Sechenov, V.M. Bekhterev, and I.P. Pavlov did not concern themselves directly with experimental solution of this problem and their conclusions had a theoretical character, being based on the experimental data and clinical observations of other researchers. The observations of N.M. Sokovnin (1877) are of exceptionally great importance among the physiological investigations that formed the basis for the modern theory of peripheral, or local reflexes. After a thorough analysis of the available literature on the mechanisms by which the elimination and retention of urine are controlled, Sokovnin stated: "All other factors apart, Afanas'yan's investigations showed that movements of the bladder can be made without cerebral participation; the source of these contractions must consequently be sought in the spinal column and the sympathetic ganglia." Sokovnin therefore set himself the task of making an experimental study of these two possible mechanisms for regulating urination.

He described his experimental method on the following manner: "The abdomen of a curarized cat was opened and the inferior mesenteric artery was taken where it rises from the aorta, tied off at two points, and cut between the ligatures. The peripheral branch of the artery was drawn up slightly with the aid of one of the ligatures. This procedure enabled us to use a pair of fine scissors to isolate the inferior mesenteric ganglion from above and laterally, leaving intact only the ganglion itself and its two branches to the hypogastric plexus (a postmortem examination was made in each case to check that the ganglion had been completely isolated from all its other connections). One of these two branches was then tied off close to the hypogastric plexus and transected below the ligature. I thus obtained the rather long, completely isolated central end of the nerve to be studied." In order to keep current division from influencing the results yielded by electrical stimulation, Sokovnin made control observations with ligatures in place, using a physiological rheoscope. These observations showed that the physiological data were completely reliable.

N.M. Sokovnin's experiments established that the urinary bladder contracts when the central end of a transected hypogastric nerve is stimulated, provided that the other hypogastric nerve is left intact. This indicates that the inferior mesenteric ganglion is a reflex center. In demonstrating this Sokovnin emphasized: "It must be noted, that in order to be successful, the experiments proving this require rapid, careful isolation of the ganglion. It is also important that the bladder not be too full of urine. In any event, the bladder contractions obtained in these experiments are weaker than those produced by stimulation of the same nerve without isolation of the ganglion. This might give one the idea that the reflex under consideration is transmitted through the spinal cord as well as through the inferior mesenteric ganglion. However, this phenomenon is quite adequately explained by the inevitable loss of stimulability in the isolated ganglion and there is no need to resort to a superfluous hypothesis that is not subject to experimental verification."

N.M. Sokovnin also demonstrated the possibility of reflex transmission from the sacral sensory fibers to the urinary bladder through the spinal cord and emphasized that the spinal center, which functions reflexively, "can probably be excited conjointly with the inferior mesenteric ganglion by wave-like impulses from the brain." The fact that the reflex activity of an autonomic ganglion depends on the brain had thus already been noted in 1877.

We have given so detailed a description of N.M. Sokovnin's research method and results for a number of reasons. First, our description of his experimental method clearly shows that it was quite advanced. Despite the fact that more than 80 years have elapsed Sokovnin published his results, various modifications of the method he developed are still being successfully employed for physiological observation of the activity of the inferior mesenteric ganglion, the urinary bladder, the prostate gland, and other organs of the true pelvis.

In particular, N.M. Sokovnin is considered to be one of the discoverers of the phenomenon that subsequently came to be called the "axon reflex." Ignorance of his research caused some investigators to make serious errors in their evaluations of the peripheral mechanisms of neural regulation. Sokovnin was one of the founders of the modern theory of peripheral, or local reflexes, but had nothing to do with the theory of axon reflexes.

The results of N.M. Sokovnin's observations were confirmed by the investigations of Nussbaum (1879), F.M. Openkhovskiy (1888), V.M. Rozhanskiy (1889), L.B. Popel'skiy (1900), E.V. Erikson (1900), Laignel-Levastine (1903), and others. According to Navrotskiy and Skabichevskiy (1891), the hypogastric nerves from the urinary bladder contain sensory sympathetic fibers whose reflex center is the inferior mesenteric ganglion.

V.L. Borman (1898) found that ligation of all the nerve branches linking the inferior mesenteric ganglion to the spinal chord does not disrupt prostate secretion when the central end of a transected hypogastric nerve is stimulated, provided that the other hypogastric nerve is left intact. This phenomenon was described by N.A. Mislavskiy and V.L. Borman (1898). They hypothesized that the hypogastric nerve has two reflex arcs for the prostate gland: one is completed in the spinal cord and the other in the inferior mesenteric ganglion. In 1926 I.V. Domrachev confirmed the validity of this hypothesis, but found that when the pathways joining the inferior mesenteric ganglion to the spinal cord are left intact stimulation of the central end of a hypogastric nerve greatly stimulates prostate secretion in comparison with the level observed when these connections are completely severed. Thus, in 1926 Domrachev noted the same phenomenon for the reflex regulation of prostate activity that N.M. Sokovnin had reported in 1877 for the reflex regulation of bladder activity.

A.I. Yushchenko (1898) regarded the inferior mesenteric ganglion both as a reflex center and as a center that inhibits automatic movements of the bladder. Courtade and Guyon (1897) and A.E. Leman (1912) pointed out that rectal reflex arcs may be completed in the inferior mesenteric ganglion.

Toward the end of the 19th century the conclusion of physiologists regarding peripheral, or local reflexes received further substantiation from morphologists. A.S. Dogel's histological observations (1896) established that the intestinal wall contains nerve cells, which he designated as sensory. The dendrites of these cells terminate in the intestinal mucosa, while their neurites terminate on the somae of motor neurons. Such cells are now known as Dogel' cells of the second type. The operative method employed at the Kazan' Histological School played an important role in the study of these cells. Thus, Dogel' cells of the second type are more stable in intestinal-wall transplants than cells of the first type. This difference may be associated with the functional characteristics of the two types of cells (I.F. Ivanov, 1937). Transection of a nerve trunk does not cause degeneration of all the fibers in the peripheral end. The somae of the nondegenerating fibers (neurites) consequently lies in the intestinal wall (I.F. Ivanov and T.N. Radostina, 1935). The course of such fibers with somae in the intestinal wall can be traced to the solar plexus and they may be linked both to the intramural Dogel' cells of the first type and, by their dendrites, to the paravertebral ganglia. The ratio of the number of Dogel' cells of the second type to the number of nondegenerating fibers at appropriate points in the intestine confirms that the nondegenerating fibers actually rise from Dogel' cells of the second type (I.F. Ivanov, 1937). There is thus every reason to assume that cells of the second type are the morphological substrate for the receptor element of a local reflex arc.

The histological investigations of N.S. Kondrat'yev (1934) showed that, in addition to the nerve tracts linking them to one another through the central nervous system, all the abdominal organs have shorter connections, which form the subperitoneal plexus. This plexus incorporates nerve tracts with an without intermediate somae. The somae of the intermediate neurons can lie inside or outside the ganglia of the intramural plexus. In cats poisoned with toxic doses of plasmocide the intestinal-wall galgliar cells most severely damaged are those of the second type, which indicates their sensory nature (I.I. Kukolev, 1944). The sensory character of Dogel' cells of the second type was demonstrated by the investigations of N.G. Kolosov and his colleagues (N.G. Kolosov and G.I. Zabusov, 1944; I.I. Kolesnichenko, 1943; N.G. Kolosov, 1948; G.A. Kablov, 1951; N.G. Kolosov, 1957; et al.). We will consider these investigations in detail after discussing the data in the literature that cast doubt on or refute the possibility of peripheral reflexes in vertebrates.

In repeating N.M. Sokovnin's experiments, Langley and Anderson (1899) divided their observations into two stages. In the first stage they transected all the nerve trunks linking the inferior mesenteric ganglion to the spinal cord and higher-lying branches of the sympathetic nervous system. In the second stage, after fiber degeneration, they stimulated the central end of a hypogastric nerve, which did not cause reflex contraction of the bladder muscles. On the basis of their experimental results, these authors concluded that the reason for the contraction of the bladder muscles on stimulation of the central end of a transected hypogastric nerve (with the other hypogastric nerve left intact) in Sokovnin's experiments was not reflex transmission through the inferior mesenteric ganglion, but an axon reflex of the centrifugal preganglionic sympathetic fibers.

These experiments by Langley were the beginning of the theory of axon-reflex transmission of excitation in efferent sympathetic fibers and of the absence of conditions for reflex transmission from afferent to efferent neurons in the peripheral ganglia of the sympathetic nervous system. The sympathetic nervous system came to be regarded as consisting solely of efferent fibers. If afferent fibers were encountered in the sympathetic trunks, they entered them from other systems (spinal and cerebral). The sensitivity of the internal organs was attributed to innervation from the intervertebral spinal ganglia and the brain.

Kolliker (1902) had already suggested that the sensory innervation of the internal organs originates in the spinal ganglia, but this hypothesis was verified experimentally by B.I. Lavrent'yev and his colleagues (1946) and by other authors. In experiments involving removal of the intervertebral ganglia Lavrent'yev conclusively demonstrated that the smooth musculature of the intestine has spinal sensory innervation. Ye.K. Plechkova (1948) found that some of the sensory fibers in the heart and blood vessels belong to the depressor nerve, while the remainder belong to the 1st-3rd thoracic intervertebral ganglia. A.Ya. Khabarova (1961) established that the heart contains three afferent plexi – the bulbar plexus and two spinal plexi. The former is formed by sensory-cell dendrites from the g. jugulare and g. nodosum, while the latter is formed by peripheral dendrites from the spinal ganglia at the level of the first six spinal segments. If the posterior roots are transected from the last lumbar segment to the third sacral segment the sensory endings in the urinary bladder degenerate (Ye.K. Plechkova, 1948).

The sensory endings in the aorta degenerate after extirpation of the intervertebral ganglia on one or both sides (from the 4th to the 12th thoracic vertebra). The distribution density and structural complexity of the interoceptors decreases in the caudal direction. The number of sensory endings of spinal origin in the aorta is considerably greater than the number of endings of cerebral origin. The sensory innervation of the aorta from the spinal ganglia has a segmental character (T.A. Grigor'yeva, 1948).

I.I. Kolesnichenko (1943; working in the laboratory headed by N.G. Kolosov) detected changes in terminal nerve-fiber segments in smooth-muscle elements of the walls of the intestinal capillary network after removal of the 8th to 12th spinal ganglia. The characteristics of these fibers enable us to regard the latter as afferent with a high degree of probability. Histologists have thus demonstrated that the sensory innervation of the internal organs may be cerebrospinal in origin. This has also been confirmed by physiological observations. Moreover, the data cited do not exclude the possibility of sympathetic sensory innervation of the internal organs or the existence of reflex arcs completed in the peripheral autonomic ganglia. However, a considerable number of investigators still deny that reflex completion in the sympathetic ganglia is possible and contrast it to the axon-reflex activity of the sympathetic system.

In 1928 L.A. Orbeli emphasized that the majority of researchers recognized only axon-reflex rather than reflex activity in the sympathetic nervous system. Some authors (L.A. Koreysha, Drezel) believe that true reflexes can be effected by the peripheral sympathetic ganglia. L.A. Orbeli thought that a number of facts indicate the wide distribution of axon-reflex reactions and their undoubted participation in pathological, if not physiological vital activity.

The preganglionic and post-ganglionic efferent fibers of the sympathetic nervous system are highly ramified. A single preganglionic fiber may pass through a number of sympathetic ganglia without terminating in them, merely making contact with the gangliar cells by means of their numerous branches. As a result of an axon-reflex reaction, the excitation induced by electrical stimulation may propagate to all the ramifications of such fibers and be transmitted to many neurons, evoking reactions in the numerous organs innervated by the sympathetic system. L.A. Orbeli agreed with Krogh's 1927 statement, with respect to the axon reflexes of sensory but not efferent fibers, that axon-reflex activity is a primitive form of neural interaction characteristic of lower animals, being supplanted in higher animals by true reflex activity. The data that formed the basis for Orbeli's theoretical conclusions regarding the axon reflexes of efferent sympathetic fibers were confirmed in experiments by A.V. Tonkikh (1925, 1926, 1934), N.V. Rayeva and A.V. Tonkikh (1928), G.Ye. Stepanov and Ye.N. Speranskaya (1928), Ye.N. Speranskaya-Stepanov (1925, 1926), and certain other researchers.

In experiments on frogs A.V. Tonkikh (1925, 1926) found that, despite preliminary destruction of the brain and spinal cord and disengagement of the adrenal glands, the heart rate rises when the central end of a transected splanchnic nerve is stimulated. This effect disappears if both vagal sympathetic trunks are transected in the cervical region. In this case impulses generated by stimulation of the greater splanchnic nerve are transmitted to the heart through the sympathetic trunk and the vagal sympathetic trunk. In frogs whose central nervous systems have been destroyed stimulation of a vagal trunk severed in the cervical region causes blanching and movement of the stomach and intestine. As a result of experiments on homiotherms, A.V. Tonkikh (1934) stated that changes in cardiac activity may occur after destruction of the entire spinal cord if the central end of the transected ulnar or radial nerve or sometimes the median nerve is subjected to electrical stimulation. Tonkikh suggests that, while his establishment of an axon-reflex link between the front legs of an animal and its heart introduces nothing radically new, it is nevertheless an additional proof that axon reflexes are not artificial, but are a normal physiological mechanism that plays a certain role in physiological and, to an even greater extent, pathological processes. N.V. Rayeva and A.V. Tonkikh (1928) studied the axon-reflex transmission of impulses to the heart through the post-ganglionic and preganglionic sympathetic fibers on stimulation of the splanchnic nerves of the cat. In addition to transection of the nerves, the possibility of impulse transmission through the post-ganglionic fibers was excluded by administration of nicotine, which was injected intravenously or applied directly to the sympathetic ganglia.

Ye.N. Speranskaya-Stepanova (1925, 1926) reported that stimulation of the central end of a sympathetic trunk leading to a ganglion causes the blood vessels to dilate and constrict and the skin glands to secrete; this occurs both in the ipselateral extremity and in the corresponding segment of the opposite extremity, provided that the skin of the hind leg of the frog is innervated solely by peripheral sympathetic neurons. On the basis of these observations, Speranskaya-Stepanova concluded that the peripheral sympathetic fibers may cross. In the author's opinion, the problem of the mechanism underlying the reaction effected by the sympathetic ganglia (whether it is an axon reflex or a true reflex) is an extremely difficult one to resolve, since no special techniques have been developed for this purpose. In particular, the nerve-transection method is unsuitable for obtaining an unambiguous answer. The results of experiments involving nicotine poisoning of the sympathetic ganglia are not conclusive. No matter how carefully nicotine is applied to the ganglia, it quickly causes blocking of the excitation impulses in the fine nerve fibers.

A drawback noted by N.F. Popov and A.A. Yushchenko (1933) was the fact that the experimental results may be influenced to a considerable extent by the artificiality of the experimental conditions (anesthesia, extensive incisions in the chest and abdomen, heating of the subject, artificial respiration, etc.). These authors made their observations on animals preliminarily subjected to the operation devised by N.F. Popov in 1932 (destruction of the spinal cord below the cervical region, etc.). This preliminary operation caused degeneration of the preganglionic sympathetic fibers. Electrical stimulation of the splanchnic nerves, the abdominal sympathetic trunk, or the peripheral end of a preliminarily transected vagal sympathetic trunk did not cause changes in cardiac activity in such animals. The abdominal organs are consequently linked to the heart through the preganglionic fibers of the splanchnic nerves. The preganglionic axonal pathways to the splanchnic nerve also affect cardiac functioning, raising blood pressure. N.F. Popov (1934) made a detailed study of the condition of the autonomic functions of dogs after separation of central and peripheral neural structures. The animals were first subjected to the operations devised by Goltz and Ewald (removal of the spinal cord below the 5th-6th cervical vertebrae), Cannon (removal of the sympathetic trunks), and I.P. Pavlov (transection of the vagal sympathetic trunks at the cervical level). The animals survived for varying periods after these operations.

N.F. Popov was convinced that both central and peripheral neural structures participate in regulating autonomic functions. Being the apparatus of local regulation, the peripheral structures have an unusual direct capacity for adapting autonomic functions to the body's needs, while the central apparatus merely modifies the functions of the local apparatus. It should apparently follow from this conclusion that the peripheral neural structures operate on a reflexive principle in their regulatory activity, but Popov unfortunately does not mention this anywhere in his writings. He also fails to suggest that local neural regulation is based on local or peripheral reflexes rather than the axon reflexes of preganglionic sympathetic fibers. One may thus get the idea that the axon reflexes of efferent sympathetic fibers are the peripheral local regulatory mechanism. "Participating in the regulation of autonomic functions, the peripheral neural structures, detached from the integrating centers, exhibit autonomy, or local functioning, which is directed at maintaining the processes taking place in the tissues and organs and displays a clear tendency toward functional adaptation of the organs. They are thus not merely passive participants in the regulation of autonomic functions, as the adherence of Langley's theory usually attempt to characterize them."*

As is well known, Langley never wrote of "the activity of peripheral reflex arcs," but, quite the contrary, asserted that they do not exist at all. In his opinion, only "the axon reflexes of efferent sympathetic fibers" are active. This corresponds to L.A. Orbeli's belief that the axon reflexes of efferent sympathetic fibers participate in vital activity under pathological, if not physiological conditions.

We feel that N.F. Popov's investigations indicate that the phenomena of peripheral neural regulation that he described are based on "peripheral, or local" reflexes. However, he himself does not draw this conclusion and inclines toward the view that his observations agree with Langley's theory of the axon reflexes of efferent sympathetic fibers.

I.A. Arshavskiy's conclusions (1930) regarding the reactions of the intestine after its connections to the spinal cord have been destroyed are also contradicted by the nature of his results. S.I. Gal'perin and V.N. Chernigovskiy (1937) observed tonic contraction of the urinary bladder on electrical stimulation of the central ends of the radial and sciatic nerves after destruction of the spinal cord and removal of the adrenal glands. The reactions obtained were characterized by long latent periods, large after-effects, rapid fatigue, and an axon-reflex character. Some morphologists, particularly Stoehr (1932), Renson (1948), and others who denied the sensory nature of Dogel' cells of the second type provided considerable support for Langley's belief that reflex arcs are not completed in the peripheral sympathetic ganglia.

There is at present no unanimity of opinion among morphologists regarding the possible interconnections between peripheral sympathetic neurons. On this topic B.I. Lavrent'yev (1946) wrote: "The data that we now have available force us to approach this problem very cautiously. Comparing all the facts that speak for and against the presence of synaptic connections between peripheral neurons, we must conclude that there has still been no observation for experiment that indicates the existence of such links with sufficient conclusiveness. In prior experiments I mistook the ramifications of sympathetic cells, whose dendrites often abut on the somae of adjacent nerve cells, for pericellular apparatuses. Check experiments involving transection of the preganglionic fibers showed that this operation causes complete disappearance of the nerve-cell synapses ... it must be assumed that the peripheral neurons do not have synaptic connections to one another. Reflex phenomena can be satisfactorily interpreted in terms of the axon-reflex phenomenon."

Langley's view was shared by a number of other researchers (Renson, 1921; Freund and Sheehan, 1943; Fulton, 1945; et al.). A.A. Zavarzin (1941), who established the perceptual significance of dendrites of Dogel' cells of the second type in the arthropod heart and intestine, felt that the significance of these cells in higher animals was still unclear.

Unfortunately, research on peripheral reflexes did not come to be widely known and was discussed only from the standpoint of the axon-reflex theory. Meanwhile, data obtained in such research continued to accumulate. N.S. Vlasov (1903) pointed out that: "the principal result of our observations on operated animals is the fact that the urinary bladder, when isolated from the central nervous system, undergoes a certain cycle of disturbances of its function, the elimination of urine, which is ultimately restored to an almost-normal level."

Restoration of bladder activity after irreversible damage to the spinal cord is a well-known phenomenon in clinical and experimental practice, but its mechanism cannot be understood if the activity of the peripheral branches of the sympathetic nervous system is reduced merely to axon-reflex activity. As N.S. Vlasov notes, the restoration of bladder activity after destruction of the lumbo-sacral portion of the spinal cord can be explained only if the nerve cells in the hypogastric plexus and the bladder wall can serve a regulatory function. This is possible only during reflex activity.

I.P. Razenkov's experiments (1926) failed to confirm Langley's basic conclusion that the sympathetic nerve must retain undegenerate preganglionic fibers in order for the urinary bladder to continue reacting to stimulation of the central end of a hypogastric nerve. Razenkov preliminarily induced degeneration of these fibers, but stimulation of the central end of a hypogastric nerve continued to evoke contraction of the bladder muscles. This effect was not produced when the inferior mesenteric ganglion was smeared with nicotine before stimulation, i.e., when the possibility of synaptic transmission in the ganglion was eliminated. If all the nerve branches linking the inferior mesenteric ganglion to higher elements of the nervous system are transected, one of the hypogastric nerves is severed, and a histological examination is made of the transected trunk after waiting the requisite interval for degeneration of the fibers isolated from the nerve-cell somae, it is found to contain a large number of undegenerate fibers. The nerve-cell somae connected to the undegenerate fibers consequently lie in the inferior mesenteric ganglion, which may be a center of reflex reaction.

In addition to data yielded by observation of reactions associated with the activity of the nerve fibers passing through the inferior mesenteric ganglion, there are similar data obtained in experiments on other peripheral autonomic ganglia. L.A. Koreysha (1925) believed that reflex transmission takes place in the superior cervical sympathetic ganglion and the inferior vagal ganglion. V.V. Lebedenko (1926) noted that all sympathetic ganglia are capable of reflex activity, since they contain afferent and efferent fibers.

In our laboratory G.A. Vaksleyger (1937) studied the mechanisms by which cardiac activity is regulated during muscular work in homoiotherms. He found that in 70% of his observations tetanization of the muscles of the hind legs caused an acceleration of heart rate despite destruction of the spinal cord; however, this reaction became unstable and readily disappeared when the temperature was reduced or other conditions unfavorable to vital activity were brought to bear. It might be assumed that, under these conditions, the working muscles affected the heart only through the vascular system, but this was not so. Acceleration of the heart rate occurred in 50% of all cases when, in addition to destruction of the spinal cord, the abdominal aorta and inferior vena cava were clamped. In this case excitation may have been transmitted from the working muscles through the afferent sympathetic fibers and the lymphatic system. However, this process is effected slowly by the lymphatic system, a hypothesis confirmed by the rapidity with which changes in cardiac activity occur after muscular work begins. Prevention of impulse transmission through the sympathetic system after destruction of the spinal cord and transection of the blood vessels causes complete cessation of the cardiac reaction to muscular work performed by the hind legs.

In these experiments the stimulus to the nervous system was muscular contractions, which are capable of stimulating the endings of sensory fibers but not motor fibers, since excitation is not transmitted from contracted muscles to the endings of efferent fibers. Conditions consequently existed for a reflex reaction involving the afferent sympathetic fibers, but there was no possibility of an axon-reflex reaction of the efferent sympathetic fibers.

In work conducted jointly with V.A. Vinokurov (1950) we showed that an increase or decrease in pulmonary pressure causes formation of third-order vascular waves both before and after the central influence of this stimulus on the lungs and pulmonary vessels is eliminated. If it is assumed that the peripheral nervous system participates in the formation of third-order vascular waves, a quite permissible assumption in this case, it is scarcely possible that its participation takes the form of axon-reflex transmission. The applied pressure in the lungs can stimulate neither the endings of the efferent fibers nor the sympathetic trunks.

In our laboratory M.I. Kholodenko (1952) discovered that there is an increase in pressure in the external jugular vein and the carotid artery when the internal jugular vein on the same side is constricted with a ligature. If this reaction were effected through the central nervous system there would inevitably have been changes in pressure in the vessels on the opposite side of the neck, a phenomenon not observed. The effect in question consequently results from a peripheral vascular reflex. Ye.I. Sinel'nikov and his colleagues conducted a number of interesting and important investigations on peripheral reflexes.

In the experiments conducted by T.P. Gugel'-Morozova, D.N. Dushko, and Ye.I. Sinel'nikov (1935) on dogs and cats after destruction of the spinal cord and in those carried out by Ye.I. Sinel'nikov and T.P. Gugel'-Morozova (1937) on isolated pelvic and alimentary organs, an increased pressure in the organ in question and various chemicals were employed as stimuli. Since electrical stimulation was not used, they were able to stimulate sensory endings (receptors), but not nerve fibers or trunks. These authors found that there are peripheral neural pathways for such stimuli among all the abdominal organs, but that the extent of these associations bears a definite relationship to the system in which they are located. More pronounced reciprocal reactions are observed in the pelvic organs (uterus, bladder, rectum); equally marked reactions occur in the alimentary organs (stomach, duodenum, gall bladder). The reciprocal influences exerted by the pelvic and alimentary organs are still less pronounced.

The reciprocal reactions of the abdominal organs described by Ye. I. Sinel'nikov and his colleagues after disengagement of the central nervous system or isolation of the organs cannot be attributed to either post-ganglionic or preganglionic sympathetic axon reflexes. The impossibility of excitation transmission by post-ganglionic axon reflexes is indicated by the distance separating the aforementioned two groups of organs. There is also little reason to assume that excitation can be transmitted by preganglionic axon reflexes, especially since afferent endings rather than efferent collaterals were stimulated. The authors feel that there are true reflex pathways consisting of afferent and efferent fibers and sympathetic cells between the internal organs. That excitation is transmitted reflexively is also indicated by the following fact. If the contractions of two segments of the small intestine are recorded and the stomach or testicles are stimulated, one intestinal segment may be excited and the other inhibited. In the opinion of Ye.I. Sinel'nikov et al. (1937) the reflex arcs for a number of peripheral reflexes consist of three neurons: sensory, intermediate, and motor. One peculiarity of viscerovisceral reflexes is the fact that, unlike viscerocutaneous or visceromotor reflexes, they are not limited to one or several segments, but always have a diffuse character, extending far beyond the segments to which the innervation of the organ stimulated is linked. This forces us to assume that intrasegmental pathways exist.

B.V. Pavlov (1937) convincingly demonstrated that stimulation of various internal organs can produce viscerovisceral reflexes in the heart of a snail whose central nervous system has been destroyed.

Mechanical stimulation of the mantle skin, kidneys, or stomach may cause changes in respiration in a Roman snail whose central nervous system has been removed (G.T. Semenyuk, 1940). In experiments on crabs B.V. Pavlov (1947) found that removal of the cerebral ganglia does not eliminate viscerocutaneous and viscerovisceral reflexes in the heart, with the exception of reflexes originating in the eye stalks, which are innervated by these ganglia. Removal of the abdominal ganglion eliminates viscerocutaneous reflexes, but only attenuates viscerovisceral reflexes. The latter are retained after removal of both the abdominal ganglion and cerebral ganglia. B.V. Pavlov concludes that: "The presence of viscerovisceral reflexes in crabs after extirpation of the central nervous system gives us grounds for assuming that these reflexes may be either axon reflexes or local reflexes effected through the sympathetic plexi and the cardiac neural network and intramural elements."

In drawing their theoretical conclusions, Ye.I. Sinel'nikov and his colleagues made extensive use of the histological results obtained by N.S. Kondrat'yev, V.S. Kofman, A.A. Shabadash, and others, who demonstrated the abdominal and pelvic organs and the interorganic spaces are extremely rich in ganglia, nerve cells, and plexi (A.G. Arnshteyn, 1887, 1902; D.A. Timofeyev, 1895; et al.).

Unfortunately, Ye.I. Sinel'nikov and T.P. Gugel'-Morozova (1937) sometimes substituted the concept of "neural reticulum" for that of "neuron." It is obvious that the concept of the "neuronal structure of the autonomic nervous system" is the opposite of rather than identical to that of the "reticular structure of the autonomic nervous system." Substitution of one concept for the other confuses our notions of the structure of the autonomic nervous system and of its functional characteristics. The "neural reticulum" concept is also encountered in works by other colleagues of Ye.I. Sinel'nikov. Strict definition of the concepts of "neuronal structure" and "reticular structure" is necessary, since some researchers still defend the idea that the terminal elements of the autonomic nervous system have a reticular structure. Jabonero (1952, 1955) and Meyling (1952, 1955) established that the terminal autonomic elements consist of interstitial Cajal cells linked synthicially to Dogel' cells of the second type. The interstitial cells and the Dogel' cells consequently form a unified system.

The theory of the reticular structure of the peripheral elements of the autonomic nervous system has been repeatedly confirmed by careful experimental verification. The investigations of B.I. Lavrent'yev (1939) and his colleagues (Ye.K. Plechkova, 1939; et al.) led to the conclusion that the interstitial cells are Schwann elements forming pathways for the autonomic nerve fibers.

The results of the research of Jabonero and Meyling are similar to those obtained by N.G. Kolosov. Comparison of the experimental data obtained by Jabonero and Meyling with those of N.G. Kolosov (1958) led to the following conclusion: "It is impossible to solve so complex a problem without having available a large amount of morphological data, particularly comparative morphological data, which will make it possible to interpret correctly the role of the Dogel' cells. Comparative histological data make it impossible for me to agree with Meyling and Jabonero, who assign Dogel' cells of the second type to the network of interstitial cells, whose neural character they attempt to demonstrate, unsuccessfully in my view ... I can in no way share this opinion, since the presence of neurofibrils or Nissl bodies in the interstitial cells has never been proved."

While emphasizing the need for clear definition of the terms "neuron" and "neural reticulum," we are not denegrating the great theoretical importance of the research conducted by Ye.I. Sinel'nikov and his colleagues. It is difficult to explain their observations from the standpoint of the theory of axon reflexes in efferent sympathetic fibers.

N.M. Rudnitskiy (1931) cast doubt on the validity of L.A. Orbeli's hypothesis that viscerocutaneous reflexes are post-ganglionic sympathetic axon reflexes. In his opinion, Orbeli's assumption that visceromuscular reactions are associated with sympathetic-fiber axon reflexes is also unconvincing. Rudnitskiy refers to the system comprising "the solar plexus, the superior and inferior mesenteric ganglia, and the thoracic sympathetic ganglia" as the extraspinal tract; primary morbidity of this system can result from definite diseases of the abdominal organs, e.g., certain forms of gastric ulcers, appendicitis, etc. To support his conclusion, the author cites A.M. Grinshteyn's statement that: "In such cases (in angina pectoris, where stimulation of the urinary bladder or intestine causes blanching and sweating in both the hands and face, which reflect a change in cardiac activity) the reflex can apparently be transmitted both intraspinally and extraspinally, i.e., through the sympathetic trunk."

During the past decade great progress has been made in studying the fine structure of the sympathetic ganglia, particularly synapse formation. I.A. Chervova (1950) emphasizes the importance for cardiac autoregulation of the fact that the intramural plexus contains synaptic links between the axons of Dogel' cells of the second type and motoneurons. G.A. Kablov (1951) observed synaptic connections for the cells of the solar plexus, although they were somewhat unusual in configuration. These synapses may have the form of single or multiple pericellular apparatuses formed by the dendrites of some of the ganglial neurons on the somae of other neurons. The dendrites of two different neurons may terminate on the soma of a third neuron, while the same dendrite may terminate on several neurons located at varying distances from one another. The cells of peripheral ganglia may give rise to dendrites that form typical sensory endings in the glia and connective-tissue membrane of the ganglion and along the bundles of nerve fibers. The endings of gangliar dendrites are sometimes in contact with one another as well as with the endings of preganglionic fibers.

In analyzing the characteristics of Dogel' cells of the second type in different animals, N.G. Kolosov (1958) notes: "... by cells of the second type we now mean all sensory neurons of autonomic ganglia." They vary morphologically in different species of animals and cells of the second type from mammals and humans are not similar to analogous cells from birds, reptiles, and lower animals. "Consequently, if we do not find typical Dogel' cells of the second type in a given plexus, this does not mean that the plexus lacks sensory neurons. This is explained by the fact that a sensory neuron in a given species of animal may be quite far removed from the usual form of Dogel' sensory cell." The author calls attention to the fact that use of the Bielschowsky-Gross method alone is not sufficient for studying the characteristics of Dogel' cells of the second type, since this technique does not make it possible to trace the entire course of their peripheral dendrites or to stain their receptor endings. All this can be done by staining the cells with methylene blue by Dogel's method.

Working in the laboratory headed by N.G. Kolosov, A.A. Milokhin (1953, 1958) was able to show that there are synaptic links between receptor and effector neurons in the intestine of the lamprey, while S.G. Kul'kin (1956) established that there are synapses of this type in the ganglia of the human urinary bladder. Thus, "... morphological data now enable us to state with certainty that there are synaptic links between receptor and efferent neurons" in the peripheral sympathetic ganglia (N.G. Kolosov, 1958).

N.P. Ivanov (1957) detected complex interneuronal links in the human cardiac ganglia in cancer of the esophagus and the cardiac region of the stomach. In some cardiac ganglia the long and short dendrites of a single nerve cell form pericellular apparatuses on the somae of adjacent neurons. Simple synaptic connections formed by two adjacent cells are often observed, the pericellular apparatuses having different forms. The author emphasizes that he observed intraganglIar connections between Dogel' cells of the second type in the cardiac ganglia.

According to the data of V.I. Pilipenko (1956, 1957), the peripheral ganglia are reflex centers that play an important role in regulating organ activity.

Dogel' cells of the second type are afferent neurons. V.I. Pilipenko attempts to find differences in the sympathetic ganglia and in synapses of cerebrospinal and sympathetic origin.

In I.D. Lev's opinion (1957), the human renal plexus, in addition to pericellular apparatuses, contains neural structures similar to the special afferent structures described by N.G. Kolosov in 1953 and 1954.

M.B. Shtark (1957) believes that the splanchnic nerves are high-capacity receivers of visceral sensations. They incorporate sensory fibers of sympathetic and cerebrospinal origin, which rise from the intervertebral ganglia (from the 1st thoracic to the 3rd lumbar ganglion) and Dogel' cells of the second type in the intramural plexi of the small intestine and gall bladder. They link the abdominal organs to the sympathetic trunk and the posterior spinal roots. Intimate connections between the cells of Auerbach's plexus and capillaries are observed in cats. At the same time, the dendritic enlargements of one nerve cell terminate on the soma of another cell, which may lie at a varying distance from the first (M.V. Shepelev, 1957).

During the past 20-30 years foreign morphologists and physiologists have presented a number of proofs that the peripheral autonomic ganglia exhibit reflex activity. Specifically, Kuntz (1922, 1941, 1945, 1953) showed that there may be synaptic links among the nerve cells of the intestinal autonomic ganglia in mammals and birds. That the autonomic ganglia play a part in the completion of intestinointestinal reflexes was confirmed by the investigations of Hermann and Morin (1934) and Hermann and Jourdan (1936). That peripheral reflexes participate in the activity of the entire alimentary tract was shown by the experiments of Garry (1933), Lawson (1934), and Lawson and Holt (1937).

Kuntz and van Buskirk (1941) and Kuntz and Saccomanno (1944) demonstrated that bile secretion and intestinal motor activity are inhibited when the pressure in the small intestine and colon is increased after isolation of the solar plexus and prevertebral sympathetic ganglia from the central nervous system. All the fibers entering the solar plexus do not degenerate when it is isolated from the central nervous system. Excitation and inhibition of the plexar ganglia can be observed (Kuntz and Richins, 1949; et al.).

The experimental data of a number of Soviet investigators agree with the results of observations of the peripheral reflexes of the digestive apparatus. Specifically, I.M. Dzhakson (1949) noted a clear reflex reaction of the pyloric region of the stomach to chemical stimulation of the ileocecal region of the intestine in animals whose spinal cords had been destroyed. B.S. Kulayev (1959) found that cats whose spinal cords had been destroyed caudal to the 2nd-5th thoracic segments responded to mechanical stimulation of a segment of the small intestine retaining only neural links to adjacent intestinal areas with reflex motor reactions of both proximal and distal intestinal segments; weak stimuli caused an intensification of peristalsis, while strong stimuli attenuated it. This reaction was more pronounced in the immediately distal segment than in the immediately proximal or more distal segments.

Bozler (1949), Schwartz (1934), Hare (1941), and others reported reflex or physiological activity in the sympathetic ganglia after they were isolated from the central nervous system. Heymans and Boyckaert (1936) noted that it is possible for the ganglia of the solar plexus and sympathetic trunk to participate in vasopressor reflexes.

Soviet researchers made a great contribution in this area. G.P. Kondradi (1944) showed that peripheral reflexes participate in the regulation of vascular tonus and that the existence of local peripheral regulation of the vascular receptors does not exclude the possibility of development of true reflexes effected by the central nervous system in these structures. Since asphyxia eliminates local vascular reactions, it can be assumed that functional tissue hyperemia results to some extent from a temporary depression of peripheral vasoconstriction mechanisms. Somewhat later (1955) G.P. Kondradi used A.A. Morozova's experiments as a basis for stating that the heart itself, i.e., the local reflexes that intensify cardiac contraction when the pressure in the venae cavae rises, depends on the nervous system. In a paper presented to the 9th Congress of Physiologists in 1959, G.P. Kondradi reported that peripheral vascular reflexes are manifested both in the presence of relatively high tonus after disengagement of the central nervous system and in the pressor reactions caused by intermittent distention of the arterial system for rapid arterial injection of chemical stimulants. The effects produced in the vascular system by injection of drugs can be subdivided into: 1) peripheral reflexes developing in the receptors of the artery that carries blood to the region of the vascular channel in question; 2) peripheral reflexes developing in the arterial receptors and transmitted to other vascular regions, the heart, and, possibly, other systems of the body; 3) true reflexes completed in various elements of the central nervous system.

In experiments on a cardiopulmonary preparation, Yu.M. Gal'perin and A.I. Briskin (1960) demonstrated that local intracardiac and cardiopulmonary reflexes play an important role in the reaction to increased intrapulmonary pressure.

Identical stimulation of the gastric receptors may cause different blood-pressure reactions before and after destruction of the spinal cord. Using this as his basis, M.G. Durmish'yan (1957) suggested that the activity of the vascular system is regulated by a "complex hierarchy of reflex actions," in which reflexes effected within the peripheral ganglia are of definite importance. Despite the fact that M.G. Durmish'yan's observations duplicate those of G.P. Kondradi, these two researchers have different understandings of the relationships between "peripheral" and "central" reflexes. In M.G. Durmish'yan's opinion, the "complex hierarchy" of regulation is based on the fact that the functional characteristics of the spinal cord are "imposed" on it by the peripheral ganglia. We can scarcely agree with this interpretation of reflex interactions.

While recognizing the existence of peripheral reflexes and the great interest shown in them by a number of authors, M.G. Durmish'yan felt that it was impossible to doubt the existence of interorgan axon-reflex links, especially after the research conducted by L.A. Orbeli and A.V. Tonkikh. We will return to this hypothesis somewhat later.

In experiments on cats whose central nervous systems had been destroyed, V.V. Zakusov and O.V. Ul'yanova (1957, 1958) established that analgetics (morphine, tecodin, promedol, and phenadone) and ganglion-blocking drugs (tetraethylammonium, pentamine, and hexonium) administered in doses sufficient to suppress viscerovisceral reflexes when the central nervous system is intact eliminate peripheral reflexes (from the urinary bladder to the cecum, ileum, and large intestine, from the distal portion of the ileum to the proximal portion of the large intestine. We know that peripheral viscerovisceral reflexes are completed in specific autonomic ganglia, as is proved by the bradycardia that develops in an isolated heart under the action of veratrine alkaloids.

A number of investigations of the mechanisms of various peripheral reactions have been conducted by I.A. Bulygin and his colleagues (I.A. Bulygin, 1949, 1957, 1959; I.A. Bulygin and M.P. Kul'vanovskiy, 1959; I.A. Bulygin and L.I. Belorybkina, 1959, 1959a; I.A. Bulygin, L.I. Belorybkina, and M.P. Kul'vanovskiy, 1961; I.A. Bulygin and M.P. Kul'vanovskiy, 1961; et al.). Summarizing the results of his many years of research on the afferent pathways taken by interoceptive reflexes, I.A. Bulygin noted that, in addition to the main afferent pathways from the stomach and pelvic organs, which are incorporated into the vagus, splanchnic, pelvic, and hypogastric nerves, there are auxiliary or indirect afferent pathways, which are components of the sympathetic nervous system and pass through the extramural ganglia. These indirect pathways are formed both by the afferent neurons of the intervertebral ganglia and by the dendrites of Dogel' cells of the second type, which are joined synaptically to other sympathetic neurons. The internal organs and the cerebral cortex may be functionally linked through these pathways.

The original method for isolating the posterior half of the trunk that was developed in the laboratory headed by I.A. Bulygin merits special attention. The spinal cord is severed below the 5th-6th thoracic vertebrae and the trunk is severed below the diaphragm, the aorta and inferior vena cava being left intact and wrapped in gauze or cotton wetted with a 10-40% formalin solution (I.A. Bulygin and M.P. Kul'vanovskiy, 1961), In the opinion of the authors, who suggested this method for studying peripheral reflexes, its principal advantage lies in the fact that a sufficiently high arterial pressure for normal vital activity of the organs to be studied is maintained in the isolated posterior half of the body. This maintenance of arterial of aterial pressure at a level sufficiently high for study of peripheral neural-regulatory mechanisms is undoubtedly a great advantage over other methods for investigating peripheral reflexes, which entail a sharp drop in arterial pressure.

It seems to us that this method should produce a considerable decrease in blood pressure in the isolated half of the body, since the abdominal vessels are deprived of central tonic stimuli. However, this reservation requires experimental verification. Moreover, attention must be called to the inaccurate designation of the solution with which the authors treated the abdominal aorta and inferior vena cava: the term "formalin" refers only to a 40% formaldehyde solution, solutions of other concentrations being simply called formaldehyde solutions. If the authors employed "formalin," it would have caused intensive dehydration and mummification of the vascular tissue and severe vasoconstriction, so that the isolated posterior half of the body would have become anemic.

I.A. Bulygin, E.I. Balakhina, and M.P. Kul'vanovskiy (1961) report that they detected formation of active substances in the posterior mesenteric ganglion under the influence of distention of the rectal and bladder walls; these substances will enter a solution perfused through the ganglion. In the authors' opinion, the neurohumoral changes in the ganglion ensure execution of a peripheral reflex and simultaneously stimulate the gangliar receptors, so that information is transmitted to the central nervous system.

This information is apparently of great importance in the regulation of the extramural ganglion by the central nervous system.

The electrophysiological method, which received wide currency in various areas of physiology during the past 20-30 years, has also been employed in investigations of peripheral reflexes (Lloyd, 1937, 1939; Job and Lundberg, 1952; Brown and Pascoe, 1954; McLennan and Pascoe, 1954; Bessau, Laporte, and Planel, 1959; O.N. Zamyatina, 1957, 1959-1961; V.I. Skok, 1959; et al.). The majority of electrophysiological research was conducted on the inferior mesenteric ganglion, although some was done on the ganglia of the solar plexus. Most of the aforementioned investigators concluded that the peripheral ganglia exhibit reflex activity, although Job and Lundberg (1952) simultaneously recognized axon-reflex transmission.

V.I. Skok (1959) believes that the ganglia of the solar plexus do not effect peripheral reflexes. The pseudoreflex reactions in which they participate when the ansa n. hypoglossi is stimulated are preganglionic axon reflexes. The preganglionic fibers that effect these axon reflexes enter the ganglion through the thoracic sympathetic trunk and a connecting branch.

Among the electrophysiological investigations in which it was proved that the inferior mesenteric ganglion and the ganglia of the solar plexus exhibit reflex-completion activity, special attention is merited by the experiments of O.N. Zamyatina (1957, 1959-1961), in which it was demonstrated that the gangliar axons of the solar plexus and inferior mesenteric ganglion of the cat retain their efferent impulsation when isolated from the central nervous system. This indicates that the cells of these ganglia display tonic activity, which may result from inherent automatism and direct afferent influences from the receptors of the internal organs. After degeneration of the preganglionic efferent fibers efferent impulses develop in the hypogastric nerve on adequate stimulation of the receptors of the urinary bladder or electrical stimulation of its nerves. These data exclude the possibility that excitation is transmitted to the ganglia in an antidromic wave along the collaterals of preganglionic efferent fibers with their somae in the spinal cord. The substantial latent period of this reaction is emphasized. Zamyatina assumes that her experimental data indicate that excitation can be transmitted reflexively from afferent to efferent neurons in the prevertebral abdominal ganglia.

Of considerable interest are the theoretical conclusions of Ye.K. Sepp (1957), who thought that he had proved the existence of both intramural and extramural peripheral reflexes. He was then faced with the broad problem of establishing the upper limit of such reflexes. Analyzing the interaction of the vagus nerve with a local reflex arc, Sepp concluded that this nerve does not transmit excitation to the arc, but regulates its excitability by acting on its efferent pathway, a Dogel' cell of the first type, through its pericellular apparatus.

In a paper entitled "Further resolution of problems in the physiology and pathology of corticovisceral relationships" presented at the 8th All-Union Congress of Physiologists, Biochemists, and Pharmacologists (1955), K.M. Bykov stated: "Morphologists and physiologists (M.V. Sergiyevskiy and others) have solidly established that there are synaptic links between the neurons of peripheral ganglia. This contradicts the well-known scheme devised by Langley and his followers. Data on lower and higher vertebrates have established that there are connections between the efferent and afferent neurons of peripheral ganglia. This gives us grounds for concluding that local reflex arcs exist. A.S.

Dogel's hypothesis regarding the afferent nature of cells of the second type in the intestine has been confirmed. B.I. Lavrent'yev's assertion that the spinal fibers detected in the sympathetic trunks and plexi are conductive pathways for sensory innervation of the internal organs also remains valid. There is thus reason to re-examine the question of so-called peripheral reflexes and the links between the peripheral sympathetic ganglia and the central nervous system.

... Proof. Sergiyevskiy recently published a mass of experimental data conclusively demonstrating that the internal organs and the vessels of different regions of the vascular system interact both through the central nervous system and through the ganglia, in the manner of peripheral reflexes ...

... On the basis of the noteworthy earlier experiments conducted at the Kazan' department headed by N.A. Mislavskiy (N.M. Sokovnin, 1877; N.A. Mislavskiy and V.L. Borman, 1897; I.P. Razenkov, 1926; et al.) and the work of his own department, Sergiyevskiy correctly concludes that it is impossible to explain all the links among the internal organs observed when the central nervous system is disengaged as being due to so-called axon reflexes."

V.N. Chernigovskiy (1943) did not regard the question of the existence of true afferent fibers in the sympathetic nervous system as having been conclusively resolved, but did assume that there was every reason to expect future researchers to find a solution. In Chernigovskiy's opinion (1944), an experiment that would correctly resolve the question of whether or not peripheral reflexes exist would have to satisfy three requirements: 1) a reflex reaction effected by peripheral reflex arcs should persist after destruction of the central nervous system; 2) the stimuli employed to evoke the peripheral reflex reactions should be adequate to the receptors in question; 3) the reactions produced should reflect the principal properties of nerve centers — excitation and inhibition.

V.N. Chernigovskiy's observation is undoubtedly correct. Unfortunately, a considerable number of the experiments conducted to prove or disprove the existence of local, or peripheral reflexes in higher vertebrates have not satisfied the aforementioned requirements. That of employing adequate stimuli has quite often been disregarded. Electrical stimulation of transected nerve trunks was used in many investigations. As a result, the reactions produced could be attributed to either peripheral reflexes or the axon-reflex activity of efferent sympathetic fibers.

We wish to discuss still another cause of the contradiction and confusion in theories of peripheral neuroregulatory mechanisms. In considering the axon-reflex transmission of excitation along nerve fibers it often remains unclear whether afferent (sensory) or efferent fibers are being discussed. This very important question generally attracts no attention and many researchers equate the axon reflexes of efferent and afferent fibers. In our opinion, this must not be done.

When speaking of the axon-reflex activity of afferent fibers, we are in full agreement with A. Krog's statement that: "Axon reflexes are a primitive form of neural interaction typical of lower animals; in higher animals they are to some extent suppressed by superimposed true (cerebrospinal) reflexes, which are reactions of a higher type than axon reflexes" (cited by K.Kh. Kekcheyev, 1946). The possibility of axon-reflex activity in sensory, or afferent fibers can be regarded as proved if we take into consideration the polyvalency of their endings, the physiological characteristics of the development of excitation in these endings, the possibility of two-way conduction of excitation along a ramified fiber, and, finally, the formation of substances that are highly active physiologically.

During phylogenesis, axon reflexes were the principal neural reactions before the nervous system differentiated into sensory (afferent) and motor (efferent) neurons. However, reception must have been effected in such a nervous system. Excitation develops in the endings of the nerve fibers of the system under the influence of the external or internal environment and is transmitted along their axons to the effector organs.

The axon-reflex reactions of the nervous system no longer were dominant when differentiation occurred: two neurons with completely different functional characteristics, one afferent and one efferent, were formed from a single perceiving and transmitting neuron. As a result, axon-reflex reactions were displaced by reactions of a higher order – true reflexes. If we assume that axon-reflex reactions persist to some extent in the nervous system under natural conditions, they can therefore be retained only in that portion of the nervous system at a lower level of evolutionary development, i.e., in the perceptual sphere, the afferent neurons.

Axon-reflex transmission of excitation along afferent fibers can occur both under experimental conditions and under natural physiological or pathological conditions. When we hear the assertion that axon-reflex transmission of excitation along efferent sympathetic fibers may be important under physiological conditions and especially so under pathological conditions, it seems improbable and unconvincing, despite its categorical nature.

There arises the question of under what natural conditions (physiological or pathological) axon-reflex activity can occur in efferent sympathetic fibers and other fibers. Excitation moves from the center to the periphery in an efferent neuron under natural conditions (physiological or pathological). No investigator has as yet discovered a single fact that indicates that excitation can be transmitted along the path "effector – efferent ending – efferent fiber," even under natural pathological conditions. Quite the contrary, it has been solidly established that transmission through the synapses of efferent neurons is uniformly one-way. Since there are no natural conditions that permit direct development of excitation in efferent endings or efferent fibers, there can be no axon reflexes in efferent sympathetic fibers. In order for an axon reflex to develop it is necessary that excitation travel from the nerve endings to the nerve soma, but the one-way conduction of their synapses makes such travel impossible in efferent neurons.

Under natural conditions, axon-reflex transmission in efferent sympathetic fibers would be possible only if they were simultaneously efferent and afferent, i.e., if their synapses did not uniformly transmit excitation only along the path "efferent fiber – effector." However, in this case the sympathetic nervous system would have a diffuse structure rather than a gangliar and truncal structure.

Russian and Soviet histologists and a number of foreign authors have established that the sympathetic nervous system has a neuronal structure and there are no morphological or physiological grounds for identifying it with the physiological characteristics of the diffuse nervous system of lower invertebrates.

In support of the theory of one-way conduction of excitation in efferent sympathetic neurons, it is pertinent to cite a statement made by L.A. Orbeli (1935) in correcting Kenkoure's theory of vasodilators: "We must imagine the posterior root as consisting of a sensory fiber and a second, efferent fiber terminating at the same cell, the soma of a sensory neuron. This scheme is in complete harmony with Kenkoure's ideas and with the physiological data presently available, which were cited by Baylis to support his views. In this case we would have an efferent fiber rising independently from the spinal cord and a discontinuity in the peripheral ganglion, as occurs throughout the remainder of the autonomic nervous system."

This statement of Orbeli's renews the dispute over the transmission of excitation from efferent to afferent fibers in the central nervous system. Shifting the process from the central nervous system to an intervertebral ganglion does not alter the nature of the question. It is just as impossible for excitation to be transmitted from an efferent to an afferent neuron in the intervertebral ganglia as in the spinal cord.

Secondly, it appears that a sympathetic neuron may have nonuniform functions not inherent in an efferent neuron, since we are speaking not of the adaptive-trophic action of a sympathetic neuron on a spinal sensory ganglion, but of the transmission of excitation from an efferent sympathetic neuron to an afferent spinal neuron. Efferent sympathetic fibers can exhibit axon-reflex activity only under experimental conditions, when sympathetic endings or trunks (the latter frequently being employed) are subjected to artificial (e.g., electrical) stimulation. Under these conditions, the two-way conductivity of the nerve fibers undoubtedly causes the excitation induced to propagate to all branches above and below the stimulation site. However, this phenomenon is not encountered under the natural conditions (physiological or pathological) of vertebrate existence.

Axon-reflex transmission of excitation in afferent fibers is thus the dominant physiological phenomenon in neural reactions at certain stages of the development of the nervous system; it is subsequently downgraded by the increasing importance of true reflex reactions.

Axon-reflex transmission of excitation in efferent sympathetic fibers is a product of artificial experimentation in physiological laboratories and not a physiological or pathological phenomenon.

Having discussed certain investigations of peripheral, or local reflexes and of axon reflexes, we should not that comparative physiological data also indicate the possibility of synaptic links between peripheral neurons of the sympathetic nervous system. The reflex reactions of invertebrates follow both long and short paths. Some of the ganglia on these pathways regulate muscular tonus and reflex activity, while others are concerned solely with reflex activity. In this connection, we conclude with the question asked by Ye.I. Sinel'nikov and T.P. Gugel'-Morozova (1937): "Can we say that, through the evolution of the nervous system, the ganglia of the vertebrate autonomic nervous system have lost their functions as tonus regulators and reflex centers?"

It seems to us that there are no experimental ground for asserting that the vertebrate peripheral sympathetic ganglia have lost their reflex function. Moreover, the available data on the reflex function of the peripheral ganglia are inadequate and require systematization.

While the axon-reflex function of afferent nerves is a physiological phenomenon, it bears no relationship to the activity of the peripheral sympathetic ganglia. As was noted in the introduction, our investigations of peripheral neuroregulatory mechanisms have extended over a comparatively long period and are intended to study the mechanisms of the peripheral reactions to changes in pressure in the abdominal blood vessels.

We will consider our research method in detail when discussing our observations: Here we will note only its general characteristics. The overwhelming majority of the experiments conducted in our laboratory were devoted to studying the influence of changes in the physiological pressure limits in isolated segments of arteries and veins and in cer- cavernous abdominal organs retaining their neural linkage to surrounding tissues on the contractile activity on the internal organs and the secretion of urine, bile, and lymph. In our opinion, the mechanical stimulus employed, an increased pressure (within physiological limits) in the blood vessels and cavernous organs, is indisputably an adequate method of stimulating the receptors of these structures. This stimulation method has definite advantages over others.

Since electrical stimulation generally excites the endings of both afferent and efferent fibers, we employed this type of stimulation rather infrequently. When electrical stimulation is utilized it is very difficult to determine whether the reactions obtained are true reflexes or axon reflexes. We employed chemical stimuli in only a very few observations. Chemical stimulation may yield results too ambiguous for interpretation of the mechanism of the reactions produced. Moreover, there may be some doubt that all the branches rising from the isolated segment of the blood vessel have been severed, particularly in connection with the difficulty of transecting all the vasa vasorum supplying the vascular walls. We felt that increasing the pressure in the isolated vascular segment would make it possible for the test substances to penetrate these extremely fine vessels.

L.M. Ishimova (1958) showed that drugs injected into an isolated artery under even slight pressure penetrate rapidly through the arterial wall (when one end of the vessel is clamped) and may spread along the nerve trunks innervating the artery. There is consequently a danger that drugs injected into an isolated vessel will enter the blood stream and have a general effect. In the course of our experiments we quite soon found that the reactions in which we were interested had a rather long latent period. However, when chemical stimulation is employed it remains unclear as to whether the duration of the latent period is associated with the structural characteristics of the apparatus that transmits excitation to the effector (the reflex arc) or with the effect of the drug as it penetrates from the isolated artery into the blood stream. The methods recommended by B.Z. Sirotin (1954, 1955) and O.P. Minut-Sorokhtina and B.Z. Sirotin (1957) for keeping drugs from penetrating the wall of an isolated vessel can be used only when observing reflex reactions effected by the central nervous system, not being applicable for observation of those of the peripheral ganglia. We also avoided perfusion of the isolated arteries, since this complicates recording of the phenomena observed.

Manuscript Page No.	[Footnotes]
22	I.P. Pavlov. Lektsii po fiziologii. 30th lektsiya [Lectures on Physiology. 30th Lecture]. Leningrad, 1952, pages 217-218.
32	N.F. Popov. Fiziologicheskiy zhurnal SSSR [Physiology Journal of the USSR], 1934, 17, 3, page 631.

Chapter 3

OBSERVATIONS ON ISOLATED PELVIC AND DIGESTIVE ORGANS

In 1940 A.P. Golovin, working in our laboratory, repeated the experiments of Ye.I. Sinel'nikov and T.P. Gugel'-Morozova in one series of observations and somewhat modified these experiments in another series. He conducted a total of 34 experiments, 27 on isolated internal organs of cats and seven on isolated organs of dogs.

During the isolation of abdominal and pelvic organs the animals were kept under general anesthesia (with a mixture of ether, chloroform, and alcohol). In performing this operation special attention was paid to retaining all the links between the isolated organs, the inferior mesenteric ganglion also being left intact. In some experiments a suture was placed beneath the ganglion and later used as a ligature when the experimental procedure so required. In such cases the ligature was applied to isolate the ganglion without mechanically affecting the complex of isolated organs.

The isolated organs were placed in a glass vessel of sufficient capacity filled with Tyrode's physiological solution heated to 38° and plentifully supplied with oxygen. The contractions of the rectum, segments of the large intestine, and urinary bladder were recorded by water-air transmission through the lever of a Marie capsule, while those of the uterus were recorded with Engelman levers. We generally recorded only the activity of those organs from which we were attempting to obtain a reflex response. In the organs of males we studied the reciprocal reactions of the bladder and rectum, while in the organs of

Fig. 1. Contractions of isolated large intestine. The arrows indicate the beginning and end of the period for which the pressure in the bladder was raised to 7 cm H_2O.

females we studied those of the uterus and bladder and of the uterus and large intestine or rectum. Stimulation was effected by increasing the pressure in one of the isolated organs by filling it with physiological solution (with manometer monitoring). The joint reactions of the isolated organs to adequate stimulation varied rather widely.

In one experiment (Fig. 1) we isolated the bladder and large intestine of a cat. We recorded the movements of the intestine when the bladder was connected to a pressure vessel and manometer through a cannula introduced into the urethra. At the beginning of the experiment (Fig. 1) the pressure in the bladder was zero and there were pronounced contractions of the large intestine. When the bladder was filled with physiological solution to a pressure of 7 cm H_2O, the muscles of the intestine exhibited an initial loss of tonus followed by cessation of contraction. Reducing the pressure in the bladder to its initial level caused a slight, brief decrease in the muscle tonus of an isolated intestinal segment; this tonus then exhibited a sudden sharp rise and intestinal motor activity was restored.

Increasing the pressure in the bladder to 7 cm H_2O thus inhibited the contractions of the large intestine and reduced its muscular tonus; reducing the pressure increased the tonus and contractile activity of the intestine. Conversely, in other cases increasing the pressure in the bladder stimulated peristaltic activity in the large intestine (Fig. 2). A.P. Golovin obtained similar results in other experiments. Moreover, the large intestine did not always react noticeably to changes in bladder pressure. Specifically, there was generally no pronounced reaction of an isolated segment of the large intestine when the pressure in the bladder was raised slowly. As A.P. Golovin correctly noted, this phenomenon is a special case of the general mechanism by which excitable tissues react to a slow increase in stimulus strength.

Fig. 2. Contraction of isolated large intestine. The arrow indicates a rise in bladder pressure.

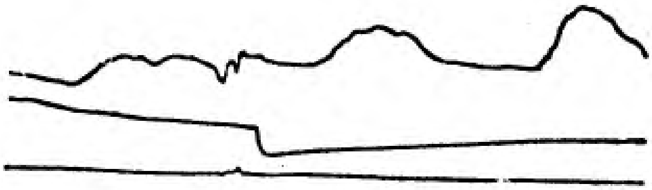

Fig. 3. Record of movements of isolated pelvic organs. The upper curve represents uterine contractions, the middle curve the change in bladder pressure, and the lower curve rectal contractions.

A variation in pressure in the large intestine may in turn be accompanied by reactions of the bladder. In one experiment on a dog we isolated a segment of the large intestine and the bladder. When the pressure in the large intestine was zero there were only slight contractions of the bladder muscles. Increasing the pressure in the intestine to 9 cm H_2O caused a sharp rise in the tonus of the bladder muscles and a substantial intensification of contractile activity. These intensified contractions of the bladder muscles ceased 2-1/2 minutes after the intestinal pressure was reduced to zero. We also observed reactions in which a rise in intestinal pressure suppressed the contractile activity of the bladder muscles. An increase in intestinal pressure can thus either intensify or inhibit bladder contractions. When isolated jointly, the bladder and a segment of the large intestine consequently exert reciprocal influences on one another. The character of the final reaction resulting from this interaction varies and depends on the initial functional state of the isolated organs. In the majority of A.P. Golovin's, a stimulatory effect occurred when the muscles of the effector organ were in a state of relative rest or exhibited only slight activity before stimulation; an inhibitory effect usually appeared against a background of more or less pronounced muscular activity in the reacting organ. When the uterus and bladder were isolated jointly a similar mechanism was observed in their interaction (Fig. 3). In an experiment on a cat we isolated the bladder, uterus, and rectum. Figure 3 shows that the uterus reacted to a slow increase in bladder pressure with vigorus contractions, which were intensified still further when the bladder pressure was sharply reduced. In this experiment the rectum did not react noticeably to changes in bladder pressure. At only one point (see Fig. 3) did the rectal muscles exhibit a low-amplitude contractile cycle, which coincided with relaxation of the uterine muscles.

There was a slow decrease in the tonus of the rectal muscles throughout the observation period.

In an experiment on a cat we isolated the uterus and bladder. The contractions of the two horns of the uterus were recorded separately as the pressure in the bladder was varied. When the bladder pressure was zero there were weak, synchronous contractions in both uterine horns. Increasing the bladder pressure to 6 cm H_2O caused inhibition of the uterine contractions. Contractile activity returned after 30 sec and continued at a faster rhythm than before stimulation. When the bladder pressure was increased to 9 cm H_2O and then rapidly reduced to zero, there was a sharp rise in uterine tonus and in the contraction frequency in both horns.

We conducted one experiment on an impregnated cat uterus, isolating the uterus, bladder, and rectum and recording the contractions of both uterine horns. The dextral horn contained two fetuses the size of a pigeon's egg and the sinistral horn contained one fetus of the same size. The pressure in the bladder and rectum was varied alternately. When the pressure in both organs was zero, the contractions of the uterine horns were powerful and rhythmic, but exhibited different rhythms in the two horns. Increasing the bladder pressure to 8 cm H_2O inhibited the contractions of both horns. This inhibition lasted for 7 min, whereupon the horns resumed contracting, despite the continued action of elevated bladder pressure. On the other hand, raising the rectal pressure to 8 cm H_2O markedly intensified the tonus of the uterine muscles and increased their contractile activity. This stimulatory effect on uterine contractions was also observed in several experiments involving an increase in bladder pressure. However, all the observations made in this area created the impression that a rise in bladder pressure has an inhibitory effect on uterine contractions. In two of A.P. Golovin's experiments the inferior mesenteric ganglia were isolated by ligation, but this did not keep the uterus from being affected by the bladder.

The neural linkage between isolated pelvic organs is consequently effected not solely by the inferior mesenteric ganglia, but also by the masses of nerve cells in the interorganic cellular tissue.

Varying the pressure in the isolated uterus may in turn intensify

Fig. 4. Contraction of isolated uterus. The arrow indicates an increase in pressure in the large intestine.

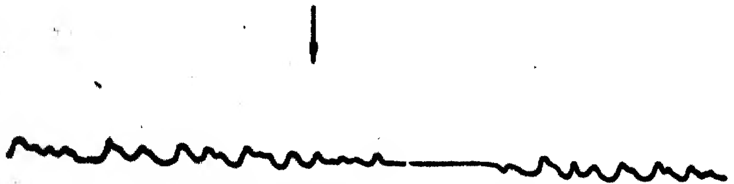

Fig. 5. Contraction of isolated uterus. The arrow indicates a rise in pressure in the large intestine.

or inhibit the motor activity of the bladder. The contractile activity of the uterus reacts in varying ways to changes in pressure in the large intestine. Specifically, in an experiment performed on 20 October 1939, an increase in intestinal pressure caused an increase in uterine tonus and a retardation of uterine contractions (Fig. 4).

Uterine contractions underwent marked inhibition in one experiment involving an increase in intestinal pressure. This is illustrated in Fig. 5.

A reaction of this type may also occur after the inferior mesenteric ganglion has been isolated. This was specifically observed in an experiment on 21 October 1939, in which we recorded the contractions of both uterine horns of a dog (Fig. 6).

The isolated uterus sometimes exhibits more complex reactions (Fig. 6a). Increasing the pressure in the rectum (first arrow at top) caused an increase in tonus and an initial intensification of contractile activity in an isolated cat uterus. The tonus then began to decrease and the cortractions became slower and of lower amplitude. The arrow at the bottom in Fig. 6a indicates a two-minute halt in the movement of the kymograph cylinder; the second arrow at the top indicates discontinuation of the elevated pressure. The uterine contractions became more frequent and stronger in response to discontinuation of the stimulus. In this experiment the stimulatory effect of the increased rectal pressure on uterine tonus thus ceased before its inhibitory effect on peristalsis.

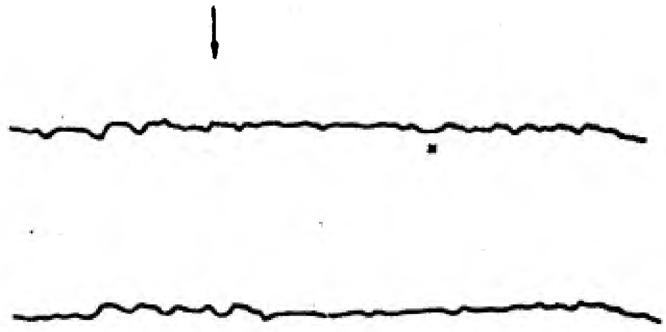

Fig. 6. Separate recording of contraction of both uterine horns of a dog. The arrow indicates an increase in intestinal pressure and the cross a decrease in this pressure.

Fig. 6a. Explanation in text.

In this series of A.P. Golovin's experiments, the isolated pelvic organs were kept in a liquid medium and were fastened rather close to one another for recording of their movements, so that the possibility of mechanical and humoral interactions between them was not excluded. In order to prevent such interaction of the isolated organs, Golovin made a second series of observations.

This series of experiments was conducted on two segments of the alimentary tract, usually segments of the small intestine joined by the mesentery. A segment of the small intestine 8-10 cm long was isolated from the abdominal cavity, special care being taken to leave the mesentery and the nerves leading to it intact. The intestinal segments were thoroughly but carefully washed in warm physiological solution and glass cannulae were inserted into one end of each segment and fastened with ligatures. The free ends of both segments were tightly tied off. The segments were filled with warm Tyrode's solution, transferred to a vapor bath at a temperature of 38°, and mounted to permit recording of their contractions. The cannulas inserted into the lumens of the segments were connected through rubber tubes to Marie capsules, whose levers recorded the peristaltic movements of the isolated segments. This experimental set-up completely excluded the possibility of humoral and mechanical interactions between the isolated organs, since they were not in contact with one another and there was no liquid between them.

We will now give a few brief extracts from the records of the experiments.

In an experiment on a cat we isolated two segments of the small intestine joined by the mesentery. Shortly after the segments were placed in an oxygen-saturated vapor bath at 38° we began to observe waves of contractions, which did not coincide in the two preparations. These contractions disappeared after approximately two min. We then stimulated one of the isolated intestinal segments mechanically and, as can be seen from Fig. 7, the initial motor activity of the stimulated segment propagated to the other segment after 24 sec. The contractions of the second segment were weaker than those of the first. The contractions of both segments ceased simultaneously and did not reappear for 5-6 min.

Subsequent electrical stimulation of the first segment caused a series of contractions in it and, after 30 sec, the second segment, which had not been directly stimulated, began to contract. The contractions of both segments again terminated simultaneously (Fig. 8). In both cases the electrical or mechanical stimulation was halted as soon as the reaction of the stimulated intestinal segment became noticeable.

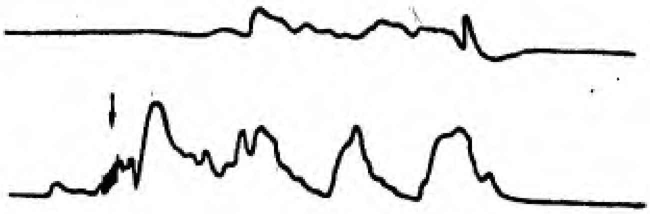

Fig. 7. Record of movements of two isolated segments of small intestine joined by mesentery. Explanation in text.

Fig. 8. Record of movements of two isolated segments of small intestine joined by mesentery. Explanation in text.

In an experiment conducted on 23 October 1940, one segment was cut from an isolated cat intestine 2 cm below the duodenum, while a second segment was cut 12 cm below the first. After being placed in a vapor bath, the first segment produced scarcely noticeable contractions, while the second exhibited somewhat more pronounced contractions. Figure 9 shows the activity of both intestinal segments.

A mechanical stimulus (pressure waves) was applied to the second segment for 26 sec. The contractions of the first segment became stronger and stronger during the stimulation period. After the stimulus was discontinued, the contractions of the second segment became even

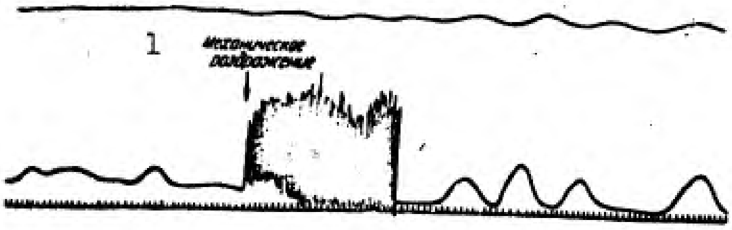

Fig. 9. Record of contraction of two isolated segments of small intestine joined by mesentery. Explanation in text. 1) Mechanical stimulation.

more pronounced than they had been before stimulation, while those of the first segment were intensified still further. It is thus important to note that the peristalsis produced in two isolated intestinal segments by stimulation may not only persist but become stronger in both segments after stimulation ceases. This phenomenon becomes comprehensible if it is attributed to nervous activity, i.e., if it is effected by a reflex mechanism that is capable of carrying out rhythmic reactions.

If this phenomenon is attributed to the axon-reflex activity of afferent or efferent nerve fibers, its mechanism remains completely incomprehensible.

A.P. Golovin obtained similar results in the other experiments of this series. In those experiments in which the stomach was one of the isolated segments of the alimentary tract, filling it with Tyrode's physiological solution and increasing the gastric pressure generally caused peristalsis to develop or be intensified in the intestinal segment isolated jointly with the stomach (and joined to it by the mesentery).

The complex of investigations carried out by A.P. Golovin thus confirms the results of the investigations conducted by Ye.I. Sinel'nikov and his colleagues. Isolated pelvic organs joined to one another by cellular tissue and isolated segments of the alimentary tract joined to one another by the mesentery may continue to interact after they have been completely isolated from the body. This interaction of isolated organs is effected through the peripheral nervous system. Variations in pressure in an isolated pelvic organ or an isolated segment of the alimentary tract (which are adequate stimuli for the receptors when kept within physiological limits) inevitably cause changes in the activity of jointly isolated pelvic organs or segments of the alimentary tract. Rhythmic activity induced in one organ by various methods leads to formation of similar activity in other organs.

The reciprocal reactions produced are rather diverse. When the pressure in one organ is increased or reduced, the activity of the other organs isolated with it may be inhibited or intensified. An initial stimulatory reaction can be succeeded by an inhibitory reaction and, conversely, an initial inhibitory reaction can be succeeded by a stimulatory reaction. Muscle tonus can be reduced or intensified. When one pelvic organ is subjected to adequate stimulation, two other organs can exhibit identical or opposite reactions, both being inhibited or excited or one being inhibited and the other excited. However, reactions of the same type are observed more frequently. These reactions have prolonged latent periods.

The complex manner in which such reactions develop refutes the possibility that they are effected by the axon reflexes of afferent and efferent fibers. In order to admit the possibility that these reactions are effected by the axon reflexes of efferent sympathetic fibers, we must assume that the endings of such fibers can be excited by a stimulus adequate to excite the receptors of sensory neurons, i.e., that the endings of efferent sympathetic neurons react in a manner physiologically similar to the endings of afferent neurons. There is, however, no factual basis for such an assumption. The complexity and variability of the reactions observed refute the possibility that they are effected by the axon reflexes of afferent neurons.

The only explanation remaining is that these reactions are effected by peripheral, or local reflexes. The pelvic organs, the cellular tissue surrounding them, and the alimentary tract are extremely rich in neurons, ganglia, and plexi. This complex morphological structure explains the diversity of the reactions observed in pelvic organs and segments of the alimentary tract when they are isolated from the body. Judging from the characteristics of the reactions observed in isolated pelvic organs and segments of the alimentary tract, the neurons of the peripheral ganglia are capable of the same basic processes, although perhaps in simpler form, as the spinal neurons (excitation, inhibition, and summation, induction, and irradiation of excitation).

Special attention must be given to the investigations of our colleague N.I. Polunin, who studied the possibility that peripheral, or local reflexes occur in lake frogs. Polunin had to accomplish the following specific tasks: 1) comparison of the reflex reactions of isolated segments of the alimentary tract before and after destruction of the spinal cord; 2) comparison of the reflex reactions of the heart and isolated segments of the alimentary tract in response to changes in pressure in one segment of the alimentary tract before and after destruction of the spinal cord; 3) comparison of the reactions of segments of the alimentary tract and the heart before and after administration of strychnine and after destruction of the spinal cord; 4) determination of the state of cardiac activity and the reactions of the alimentary tract before and after administration of hexonium.

N.I. Polunin employed the following procedure in order to elucidate these problems.

A decapitated frog was tied belly up. The body cavity was opened

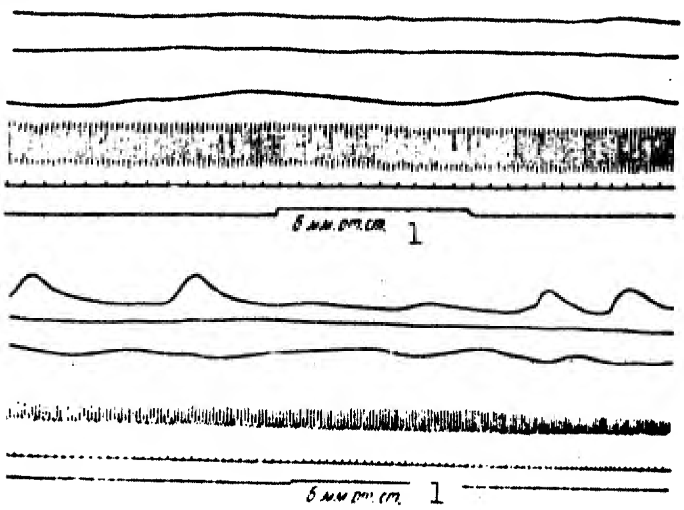

Fig. 9A. The upper curve is a record of cloacal movements, the second curve is a record of the movements of the second intestinal segment, the third curve is a record of those of the first intestinal segment, the fourth curve is a cardiogram, the fifth curve is a 5-sec time marker, and the lower curve indicates the beginning and end of stimulation. The upper six curves were recorded before destruction of the spinal cord and the lower six curves after this operation. 1) mm Hg.

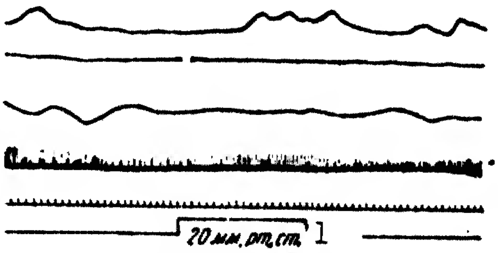

Fig. 9B. Curves the same as in Fig. 9A, except for third curve from top, which is a record of gastric contractions. Recorded after destruction of spinal cord. 1) mm Hg.

and four segments of the alimentary tract were isolated: the stomach, two segments of the small intestine (one near the stomach and the other near the terminal portion of the intestine), and the cloaca. The ends of the segments were tied off but the mesentery joining them was left intact. Sutures were used to attach the segments and the heart to levers, through which their contractions were recorded on a smoked kymograph tape. The pressure in a given segment was raised (from 5 to 30 mm Hg) by inflating it with air, using a manometer for monitoring purposes.

In one series of experiments strychnine (0.4-1 mg per kg of body weight) was injected into the subcutaneous lymph sac 10-15 min before the experiment began. In these instances the reactions of the alimentary-tract segments of animals not given strychnine served as the control. In the other series of experiments strychnine was injected into an abdominal vein after destruction of the spinal cord and preliminary investigation of the reflexes under study. In some of the experiments heparin was also administered to prevent formation of thrombi. The results obtained by I.N. Polunin are shown in Fig. 9A and B.

Figure 9A consists of two parts. The curves in the first part were recorded before destruction of the spinal cord, while those in the second part were recorded after this operation. The reaction of the isolated alimentary segments to an increase in gastric pressure was rather unclear before destruction of the spinal cord. There was a more or less distinct increase in the tonus of the first intestinal segment.

After destruction of the spinal cord an analogous rise in gastric pressure inhibited the contractile activity of the cloaca, increased the tonus of the first intestinal segment, and intensified cardiac contraction.

Figure 9B represents an experiment in which the pressure in the first intestinal segment was raised after destruction of the central nervous system. Cloacal peristaltic activity obviously participated in the response to this stimulus; cloacal and gastric tonus increased, gastric peristaltic activity being inhibited and alternating cardiac contractions (alternate strong and weak systoles) developing against this background.

Figure 9C consists of two parts. The curves in the first part were recorded before and those in the second part after destruction of the spinal cord. Roughly equivalent increases in cloacal pressure (10 and

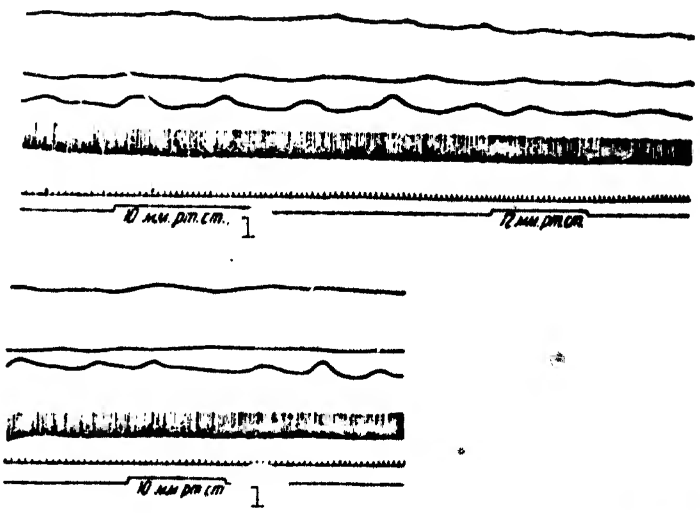

Fig. 9C. The first group of curves was recorded before destruction of the spinal cord, while the second group was recorded after this operation. The upper curve is a record of the movements of the second intestinal segment, the second curve is a record of those of the first intestinal segment, the third curve is a record of gastric movements, the fourth curve is a 5-sec time marker, and the lower curve indicates the beginning and end of stimulation. 1) mm Hg.

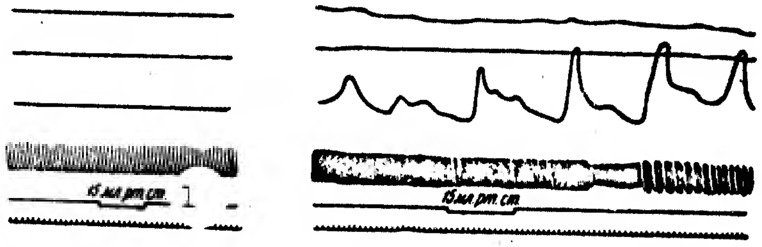

Fig. 9D. The first group of curves was recorded after destruction of the spinal cord and before administration of strychnine, while the second group was recorded after administration of struchnine. The upper curve is a record of cloacal movements, the second curve represents the movements of the second intestinal segment, the third curve is a record of gastric movements, the fourth curve is a cardiogram, the fifth curve indicates the beginning and end of stimulation, and the lower curve is a 5-sec time marker. 1) mm Hg.

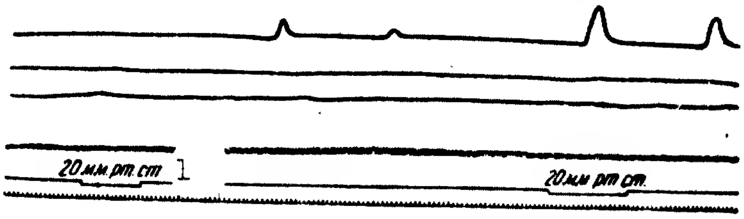

Fig. 9E. The upper curve is a record of cloacal movements, the second curve represents the movements of the second intestinal segment, the third curve represents those of the first intestinal segment, the fourth curve is a cardiogram, the fifth curve indicates application of the stimulus, and the lower curve is a 5-sec time marker. 1) mm Hg.

12 mm Hg) were employed. Before destruction of the central nervous system this stimulus intensified peristalsis in all the segments (only slightly in the first intestinal segment); conversely, after destruction of the central nervous system it inhibited the activity of all three segments. The effectiveness of the stimulus was considerably enhanced by administration of strychnine, especially in conjunction with heparin.

Figure 9D represents an experiment conducted on 12 October 1960. The first group of curves was recorded after destruction of the spinal cord and before administration of strychnine. Peristaltic activity was lacking in all the isolated alimentary-tract segments and did not appear when the pressure in the first intestinal segment was raised. The second group of curves was recorded after administration of strychnine. There were distinct changes in the muscle tonus and peristaltic contractions of the cloaca. The peristaltic movements of the stomach became quite substantial and there was a sharp increase in heart rate.

A rise in pressure in the first intestinal segment caused a considerable intensification of gastric peristalsis and a less pronounced increase in cloacal peristalsis. The frequency and amplitude of the cardiac contractions decreased slightly at first, but after 95-100 sec there was a substantial decrease in amplitude and an increase in frequency. Cardiac arrhythmia set in after an additional 60-65 sec.

Figure 9E illustrates an experiment conducted on 21 October 1960, showing the effect of varying the pressure in the isolated stomach.

The gastric pressure was first raised after destruction of the spinal cord but before administration of strychnine. The response elicited consisted of a slight increase in tonus in the first intestinal segment and, after 310 sec, strong contraction of the cloacal muscles.

A second stimulus of equal strength applied after administration

TABLE 1

Reaction of Segments of Alimentary Tract to Increased Gastric Pressure

Число отрезков пищеварительного тракта, участвовавших в реакции 1	2 Число наблюдений до введения стрихнина		5 Число наблюдений после введения стрихнина	
	до разрушения спинного 3 мозга	после разрушения спинного 4 мозга	до разрушения спинного 3 мозга 4	после разрушения спинного мозга 4
3	2	3	4	14
2	11	56	4	6
1	3	3	—	—
Не было реакции 6	1	—	—	—
Были общие движения 7	—	—	1	—
Всего. 8.	17	62	9.	20

1) Number of segments of alimentary tract participating in reaction; 2) number of observations before administration of strychnine; 3) before destruction of spinal cord; 4) after destruction of spinal cord; 5) number of observations after administration of strychnine; 6) no reaction; 7) general movements; 8) total.

of strychnine caused vigorous contraction of the cloacal muscles and induced peristalsis in both intestinal segments.

The data presented in Table 1 show that other isolated segments of the alimentary tract can react to a rise in pressure in the isolated stomach both before and after destruction of the spinal cord, simultaneous reactions of two segments predominating. The number of reactions of all three alimentary-tract segments to elevated gastric pressure increases after administration of strychnine.

Table 2 presents the results of observations made when the pressure in the first and second intestinal segments was raised.

The data on the reactions of the alimentary segments to an increase in pressure in the first intestinal segment are quite similar to those shown in Table 1. The isolated segments proved capable of reacting to a change in pressure in the first intestinal segment both before and after destruction of the spinal cord; simultaneous reactions of two

TABLE 2

Results of Observations Made with Elevated Pressure in Different Intestinal Segments

Число отрезков пищеварительного тракта, участвовавших в реакции 1	2 Число наблюдений до введения стрихнина		5 Число наблюдений после введения стрихнина	
	до разрушения спинного мозга 3	после разрушения спинного мозга 4	до разрушения спинного мозга 3	после разрушения спинного мозга 4
	9 Первый отрезок кишки			
3	6	15	11	15
2	17	22	1	8
1	8	4	1	—
Не было реакции 6	3	7	—	—
Общие движения 7	13	—	4	—
Всего. . 8	47	48	17	23
	10 Второй отрезок кишки			
3	3	2	10	20
2	2	3	7	14
1	1	6	8	4
Не было реакций 6	2	1	—	—
Общие движения 7	1	—	—	—
Всего. . 8	9	12	25	38

1) Number of segments of alimentary tract participating in reaction; 2) number of observations before administration of strychnine; 3) before destruction of spinal cord; 4) after destruction of spinal cord; 5) number of observations after administration of strychnine; 6) no reaction; 7) general movements; 8) total; 9) first intestinal segment; 10) second intestinal segment.

segments predominated before administration of strychnine, while reactions of three segments predominated after this drug was administered.

These observations thus completely confirmed the regularity of the reactions noted in the first two groups: reactions of two segments of the isolated alimentary tract predominated when the pressure in the second intestinal segment was raised before administration of strychnine, while reactions of three segments predominated after administration of strychnine. Table 3 presents the composite results of our observations of the effect of elevated cloacal pressure.

TABLE 3

Composite Results of Observation of the Effect of Elevated Cloacal Pressure

Число отрезков пищеварительного тракта, участвовавших в реакции 1	Число наблюдений до введения стрихнина 2		Число наблюдений после введения стрихнина 5	
	до разрушения спинного 3 мозга	после разрушения спинного 4 мозга	до разрушения спинного 3 мозга	после разрушения спинного 4 мозга
3	10	26	9	12
2	21	17	5	4
1	9	6	1	2
Реакции не было 6	4	2	1	2
Общие движения 7	4	—	3	—
Всего . . 8	48	51	19	20

1) Number of segments of alimentary tract participating in reaction; 2) number of observations before administration of strychnine; 3) before destruction of spinal cord; 4) after destruction of spinal cord; 5) number of observations after administration of strychnine; 6) no reaction; 7) general movements; 8) total.

The composite results of all four groups of observations indicate the existence of uniform mechanisms in the reactions of the isolated alimentary segments: 1) excitation and inhibition of activity can occur in all segments when the pressure in one is raised both before and after destruction of the spinal cord; 2) a change in pressure in one segment (most frequently the cloaca) before destruction of the spinal cord can sometimes induce general motor reactions; 3) in experiments conducted before administration of strychnine and before or after destruction of the spinal cord, a change in pressure in one alimentary segment usually causes reactions of two segments (the response to a rise in cloacal pressure is an exception to this rule, reactions of three segments predominating); 4) after administration of strychnine simultaneous reactions of three segments begin to predominate both before and after destruction of the spinal cord.

The curves presented above also indicate that these reactions become more intense after administration of strychnine. Their latent period increases after destruction of the spinal cord and decreases after administration of strychnine. The general characteristics of the reactions before and after destruction of the spinal cord and before and after administration of strychnine were similar: we observed both stimulation (manifested in acceleration and intensification of peristalsis) and inhibition (manifested in retardation, attenuation, and cessation of peristalsis and a decrease in tonus) of the activity of the isolated segments.

The reactions sometimes had a two-phase character, a stimulatory effect being succeeded by an inhibitory effect and vice versa. In many cases one or two of the alimentary segments responded with an intensification of activity, while the others exhibited inhibition. The character of the reaction depended on the initial functional state of the reacting organs in a considerable number of observations: a rise in pressure in one alimentary segment against a background of intensified activity quite often caused inhibition.

In a considerably smaller number of cases we detected a change in cardiac activity when the pressure in the alimentary segments was raised. Such instances arose before and after destruction of the spinal cord and before and after administration of strychnine. I.N. Polunin's observation thus confirm the conclusion drawn by Ye.I. Sinel'nikov and his colleagues, i.e., that intersystemic peripheral reactions are less common than intrasystemic or intraorganic reactions.

I.N. Polunin subsequently investigated the effect of administration of hexonium. A total of 0.5 ml of a 5% hexonium solution was administered before and after destruction of the central nervous system and before and after injection of strychnine (in different experiments) into the peripheral segment of the sinistral aortic arch, at the point peripheral sympathetic ganglia may effect reflex reactions, we decided to study the reaction of the urinary bladder to variations in pressure in an isolated segment of the inferior mesenteric artery and to injection of acetylcholine into this artery. The study of the innervation of urinary bladder, the regulation of urination, reflexes extending from the urinary bladder to other organs and systems, and the cortical regulation of bladder activity has to a considerable extent been conducted by Russian and Soviet researchers (Ye. Afanas'yev, 1869; N.M. Sokovnin, 1873-1877; I. Nussbaum, 1879; Navrotskiy and Skabichevskiy, 1891; V.M. Bekhterev and N.A. Mislavskiy, 1888; N.S. Vlasov, 1903; D.V. Polumordvinov and I.P. Razenkov, 1915; I.P. Razenkov, 1926; K.M. Bykov, 1941; L.A. Orbeli, 1941; M.V. Sergiyevskiy, 1929; et al.).

The inferior mesenteric ganglion, which has been studied and described by many researchers (I.M. Sokovnin, 1873-1877; Nussbaum, 1879; Navrotskiy and Skabichevskiy, 1891; A.I. Yushchenko, 1898; V.L. Borman, 1898; N.A. Mislavskiy and V.L. Borman, 1898, Courtade and Guyon, 1897; A.E. Leman, 1912; A.P. Razenkov, 1926; I.M. Domrachev, 1926; et al.), is regarded as the peripheral reflex center for the pelvic organs (urinary bladder, prostate gland, large intestine, etc.). Doubt was cast on the validity of this conclusion by the investigations of Langley and Anderson (1893), who denied the existence of peripheral reflexes in the higher warm-blooded animals and advanced the theory of axon-reflex regulation of organic vital activity by preganglionic efferent sympathetic fibers.

Langley and Anderson's view is still shared by many researchers, despite the experiments of I.P. Razenkov (1926), which led to conclusions that contradicted Langley's theory. One reason why there is still no clear solution to this problem is the lack of a suitable experimental technique. In order to evaluate the functions of the inferior meswhere it joins the dextral aortic arch. There was a brief initial intensification of the background peristalsis of the isolated alimentary segments and an intensification of cardiac activity. Hexonium also had a stimulatory effect against a background of substantially intensified peristalsis induced by preliminary administration of strychnine. The peristalsis of the alimentary segments then became less pronounced or ceased entirely. Administration of strychnine did not restore it. Raising the pressure in one of the alimentary segments failed to alter motor activity in the other segments or to stimulate cardiac activity.

The synaptic paralysis induced by hexonium in the peripheral autonomic ganglia thus led to attenuation or cessation of alimentary peristalsis and cessation of the reactions of the isolated alimentary segments to a rise in pressure in one segment. I.N. Polunin employed stimuli adequate for the mechanoreceptors and the reactions described therefore could not have resulted from the axon-reflex activity of efferent sympathetic fibers.

The reactions described by A.P. Golovin and I.N. Polunin as occurring after destruction of the central nervous system were apparently based solely on peripheral, or local reflex arcs; this was confirmed by the experiments in which strychnine and hexonium were administered. Strychnine is known to intensify the reflex activity of the central nervous system, improving its synaptic conductivity. It can be assumed that the intensification of peristalsis and motor reactions after destruction of the spinal cord and administration of strychnine resulted from an improvement in the synaptic conductivity of the peripheral reflex arcs and, conversely, that the cessation of peristalsis in response to adequate stimulation after administration of hexonium resulted from synaptic paralysis of these reflex arcs.

Chapter 4

REACTIONS OF THE URINARY BLADDER TO CHANGES IN PRESSURE IN THE INFERIOR MESENTERIC ARTERY

It is noteworthy that peripheral ganglia and plexi located near a large blood vessel and having fibers extending to it also supply fibers to organs lying a considerable distance away. The inferior mesenteric ganglion lies in close anatomic proximity to the inferior mesenteric artery and supplies fibers to the pelvic organs (urinary bladder, prostate gland, uterus, etc.). The superior mesenteric ganglion, the solar plexus, and the vessels and organs of the upper and central portions of the abdomen exhibit roughly the same anatomic relationships.

Morphological relationships of this type served as a basis for hypothesizing that there are facilities for the transmission of neural signals regarding local changes in the vascular system (fluctuations in blood pressure, chemical changes in the blood, and contraction and relaxation of the vascular walls) to the organs associated with a given portion of the vascular system, being linked to it by peripheral ganglia and plexi, and, conversely, that there are facilities for the transmission of signals regarding changes in these organs (primarily in metabolism) to the corresponding regions of the vascular system. The origins of the celiac and superior mesenteric arteries are rich in receptors (Nonidez, 1947; V.M. Godinov, 1948; et al.).

In order to check the validity of the hypothesis that the nervous system may transmit reciprocal signals regarding local changes in the vascular system and the internal organs and of the hypothesis that the

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peripheral sympathetic ganglia may effect reflex reactions, we decided to study the reaction of the urinary bladder to variations in pressure in an isolated segment of the inferior mesenteric artery and to injection of acetylcholine into this artery. The study of the innervation of urinary bladder, the regulation of urination, reflexes extending from the urinary bladder to other organs and systems, and the cortical regulation of bladder activity has to a considerable extent been conducted by Russian and Soviet researchers (Ye. Afanas'yev, 1869; N.M. Sokovnin, 1873-1877; I. Nussbaum, 1879; Navrotskiy and Skabichevskiy, 1891; V.M. Bekhterev and N.A. Mislavskiy, 1888; N.S. Vlasov, 1903; D.V. Polumordvinov and I.P. Razenkov, 1915; I.P. Razenkov, 1926; K.M. Bykov, 1941; L.A. Orbeli, 1941; M.V. Sergiyevskiy, 1929; et al.).

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Langley and Anderson's view is still shared by many researchers, despite the experiments of I.P. Razenkov (1926), which led to conclusions that contradicted Langley's theory. One reason why there is still no clear solution to this problem is the lack of a suitable experimental technique. In order to evaluate the functions of the inferior mesenteric ganglion one must resort to transection of one of the splanchnic nerves and electrical stimulation of its central end. The bladder contractions produced by such stimulation can with equal ease be attributed to reflex transmission through the inferior mesenteric ganglion or to axon-reflex transmission through the preganglionic sympathetic fibers of the hypogastric nerve.

Taking this into consideration, we decided to employ only stimuli adequate to the endings of afferent nerves (fluctuations in pressure in an isolated arterial segment) in our experiments. Changes in pressure, especially variations in arterial pressure within physiological limits, cannot stimulate the endings of efferent sympathetic fibers and thus cannot induce axon-reflex reactions in them. Our investigations were conducted on 12 dogs during 1945-1946. The animals were given morphine subcutaneously before the experiments began and placed under general anesthesia (with a mixture of ether, chloroform, and alcohol) during the operative preparations or were preliminarily decerebrated. The abdominal cavity was opened. A thin-walled rubber bulb was inserted into the bladder through a small incision and connected through rubber tubes to a water manometer and a Marie capsule, whose lever recorded the changes in bladder pressure on a moving smoked kymograph tape. The bladder, with the bulb in place, was tightly closed with a purse-string suture. Before recording bladder activity the bulb was slightly inflated or filled with physiological solution heated to 37°. The pressure in the recording system was checked with the manometer and could be changed at any time through the T-tube incorporated into the system.

The inferior mesenteric artery was tied off at two places: at the point where it rises from the abdominal aorta and 4-5 cm closer to the periphery. Special attention was paid to the branches rising from the artery. If they were in the segment to be isolated they were carefully tied off. As many of the neural connections between the isolated arterial segment and the inferior mesenteric ganglion as possible were left intact; the cannula necessary for varying the arterial pressure and injecting solutions into the artery was fastened in place with a ligature at the peripheral end of the isolated segment. The segment was carefully washed free of blood with physiological solution heated to 37°, its central end was tied off, and the cannula was connected to a mercury manometer. Between the cannula and the manometer was a glass T-piece, through which the pressure in the system could be varied by the desired amount at any time.

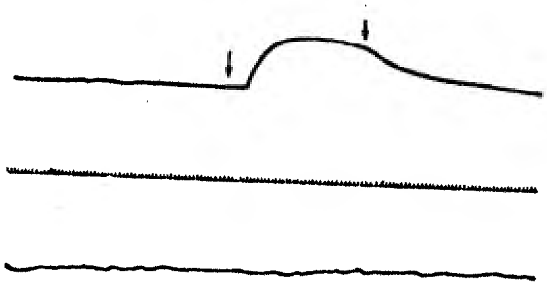


Fig. 10. The upper curve is a record of the bladder movements, the second curve is a one-second time marker, and the lower curve represents the blood pressure in the sinistral common carotid artery. Explanation in text.

The system was filled with physiological solution at 37°. One of the common carotid arteries was exposed by the usual method and its pressure was recorded with a Ludwig manometer. The experiment usually commenced 1-1-1/2 hr after the preparatory operations were completed.

In six experiments we did not observe any reaction in the bladder when the pressure in the isolated segment of the inferior mesenteric artery was varied. There were no changes in the blood pressure in the common vascular system or in respiration. In the other six experiments a rise in pressure in the isolated artery produced a typical reaction in the bladder. Figure 10 shows the character of this reaction.

Figure 10 illustrates an experiment conducted on 22 May 1945. The upper curve in Fig. 10 shows that there was a sharp rise in bladder pressure 13 sec after the pressure in the isolated segment of the inferior mesenteric artery began to rise (from an initial level of 90-100 mm to 140-150 mm Hg), while the blood pressure in the carotid artery (lower curve) remained unchanged.

In other trials in this and other experiments variations in pressure in the isolated segment of the inferior mesenteric artery caused atypical reactions in the bladder. The latent period of these reactions varied from 2-3-5 sec to 1-1-1/2 min.

Different pressures were employed in different experiments. We investigated the effect of raising the arterial pressure from 0 or 90-100 mm to 100-160-170 mm Hg. These pressures cannot be regarded as particularly high, since they are undoubtedly within physiological limits. When the pressure in the isolated artery was raised the bladder usually reacted as soon as the pressure reached 100 mm Hg or slightly more. When the pressure was raised from a base level of 90-100 mm the bladder began to react when the pressure reached 150-160 mm Hg. Therate of the rise in pressure was of great importance. Thus, when the pressure was varied slowly the bladder reaction was often entirely lacking or had a considerably greater latent period than when the pressure was raised more rapidly.

In addition to bladder reactions, larger increases in pressure produced more frequent changes in blood pressure in the common carotid artery and in respiration. The bladder muscles exhibited two distinct types of contraction. The first type is illustrated by the curve in Fig. 10. The bladder muscles responded to a rise in pressure in the isolated artery with a strong contraction, but began to relax before the elevated pressure was relieved. The second type of bladder-muscle reaction had a pronounced tonic character, which was manifested in a slow increase in bladder pressure (this pressure did not reach the level of the first variant, but the reaction persisted at the level attained for a considerable time).

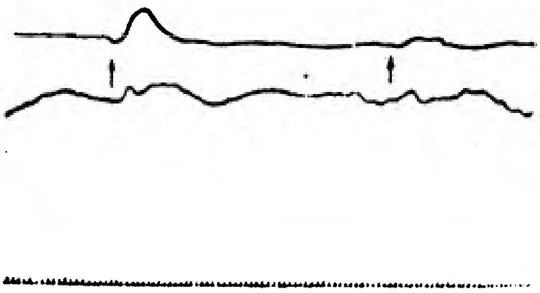


Fig. 11. The upper curve is a record of bladder contractions, the second curve represents the blood pressure in the sinistral common carotid artery, and the lower curve is a one-second time marker. Explanation in text.

We also investigated the influence of injection of acetylcholine solutions with concentrations of 1:100,000 and 1:1,000,000 into the isolated arterial segment. In a number of experiments the bladder muscles responded to injection of the acetylcholine solution by contracting after a latent period 8-11 sec in duration. The pressure in the common carotid artery either remained unchanged or varied only slightly. In any event, it was difficult to attribute such changes to the acetylcholine injection. For precisely the same reason, it was impossible to find a causal relationship between the bladder reaction and the fluctuations in pressure in the common vascular system.

The curves in Fig. 11, which illustrate an experiment conducted on 29 May 1946, showed the results of injecting a 1:100,000 acetylcholine solution.

The curves in Fig. 11 have the following characteristics. The curve representing the blood pressure in the sinistral common carotid artery exhibited third-order vascular waves. There was a vigorous contraction of the bladder muscles approximately 11 sec after the first acetylcholine injection. The blood pressure in the carotid artery also rose, but did so somewhat after the bladder muscles began to contract. The second injection of acetylcholine into the isolated arterial segment caused a weaker contraction of the bladder muscles, but the latent period was the same as in the first case. A wave-like rise in arterial pressure began before the acetylcholine was administered. Thus, even if the acetylcholine injections were responsible for the rise in pressure in the common carotid artery in both cases, the bladder reactions occurred independently of these changes in pressure.

However, the occurrence of a substantial latent period (11 sec or more) means that we cannot completely deny the possibility that the reactions resulted from drawing of the acetylcholine into the vasa vasorum and thus into the common vascular system. In all subsequent observations we consequently employed mechanical rather than chemical stimuli.

In some cases a rise in pressure in the isolated artery failed to produce a bladder reaction but a subsequent rise in pressure after administration of acetylcholine did induce a reaction, despite the fact that the solution had been removed from the artery before the pressure was increased. These observations led us to surmise that acetylcholine is capable of altering the sensitivity of the arterial receptors to mechanical stimuli.

The experiments of this group led us to conclude that mechanical (within physiological limits) and possibly chemical stimulation of the inferior mesenteric artery is capable of inducing a bladder reaction even when there are no general blood-pressure and respiratory reactions. The inferior mesenteric artery consequently contains a receptor field equipped with mechanoreceptors and possibly chemoreceptors.

Since in some cases stimulation of this receptor field can cause a local reaction, which is manifested in a change in the state of the smooth musculature of the bladder and other pelvic organs with no general arterial-pressure or respiratory reactions, we have designated this vacular receptor field as "local." This is an attempt to emphasize the functional difference between this field and the vacular receptor fields of the aorta, carotid sinuses, etc., stimulation of which always causes general changes in the functional state of the circulatory system, respiratory apparatus, etc.

The physiological significance of these phenomena is quite clear. It can be assumed that, as a result of the presence of these local vascular receptor fields, the activity of those organs linked to peripheral ganglia undergoes functional reorganization in accordance with the localization of changes in the vascular system. There is also reason to suppose that the existence of such neural links ensures local modification of circulation in accordance with primary changes in the organs.

The reactions described above persist after destruction of the spinal cord, which confirms that they may be effected by peripheral neural mechanisms. Since all our experiments utilized mechanical (elevated pressure, within physiological limits), or chemical (acetylcholine) stimulation adequate for sensory endings, we can state with certainty that the reactions were not due to the axon-reflex activity of efferent sympathetic fibers, but were effected by peripheral reflexes.

Chapter 5

REFLEXES FROM THE ABDOMINAL VESSELS TO THE SPLEEN

The structural characteristics of the spleen permit substantial changes in the extent to which it is filled with blood and this must in turn be reflected in the activity of the entire circulatory apparatus. Magandie's experiments (1830) showed that the spleen participates in circulation. S.P. Botkin (1875) noted that the filling of the liver with blood depends on the contractile activity of the spleen. Numerous researchers subsequently studied the importance of the spleen in circulation, both in experiments on animals and under clinical conditions.

In a dissertation prepared in N.A. Mislavskiy's laboratory, N.K. Koryayev (1910) made an exhaustive survey of previous investigations. He showed that this research was devoted to the effect of direct stimulation of the splenic surface, of transection and stimulation of the peripheral and central ends of the splenic nerves, of stimulation of the solar plexus and the peripheral and central ends of the transected vagus nerves, of stimulation of the cutaneous sensory nerves, the peripheral portion of the anterior spinal roots, the peripheral portion of the cervical and thoracic segments of the spinal cord, the myelencephalon, the thalamus opticus, and the cerebral cortex, and of respiratory arrest. The effects of a number of drugs (ergot, quinine, curare, morphine, chloroform, adrenal and hypophyseal extracts, etc.) were also studied.

In studying the contractile activity of the spleen, N.K. Koryayev established that both motor and inhibitory fibers are present in the splenic plexus, greater splanchnic nerve, and anterior roots of the thoracic segment of the spinal cord. However, it is considerably more difficult to observe the action of the inhibatory fibers than that of the motor fibers.

Rhythmic contractions of the spleen may continue after its connections to the central nervous system have been destroyed. Contractile activity is consequently associated with the action of a peripheral mechanism and is greatly influenced by changes in blood pressure. The reactions of the spleen before and after denervation differ. A spleen with its innervation intact reacts to a drop in blood pressure caused by cardiac arrest during stimulation of the peripheral end of the vagus nerve with an active contraction, which is often accompanied by a subsequent increase in splenic volume. The denervated spleen reacts to a sudden sharp rise in blood pressure with an active contraction, but a drop in blood pressure causes relaxation of the splenic muscles in "certain cases." N.K. Koryayev established that the denervated spleen can be made to contract by stimulating sensory nerves, this reaction being attributable to the rise in blood pressure that occurs during such stimulation.

Koryayev also noted that, in the majority of his observations, a rise in blood pressure was followed by an intensification of rhythmic splenic activity, while a drop in blood pressure was followed by attenuation of this activity. Electrical stimulation of the peripheral portion of the cervical segment of the spinal cord or of the central portion of its lumbar segment causes a rise in blood pressure and contraction of the spleen, the latter being preceded by passive distension. It can be said that the spleen reacts to artificial stimulation of the central nervous system or its trunks in the same manner as the vascular system. When stimulation causes the muscles of the vascular walls to contract the spleen also contracts and, conversely, the volume of the spleen increases when the vascular walls relax as a result of stimulation. The reactions of the spleen may deviate from this general rule in specific cases.

The hypothesis advanced in N.K. Koryayev's dissertation, that the spleen, taking in blood when it distends and expelling it when it contracts, must have a mechanical influence on circulation in the portal system, served as the starting point for the investigations of N.K. Koryayev, M.V. Sergeyevskiy, and I.I. Tsvetkov (1929), which were devoted to studying the role of the spleen in portal circulation.

The influence of the spleen on circulation in the portal system may lie in the fact that the rise in blood pressure in the splenic vein when blood is expelled from the spleen should be reflected in the pressure in the other veins of this system and may stimulate the activity of their smooth muscles. The spleen may consequently be one of the factors that stimulate the activity of the muscular walls of the veins of the portal system. The high degree of development of the splenic musculature, which has itself attracted the attention of researchers (N.K. Koryayev, M.V. Sergeyevskiy, and I.I. Tsvetkov, 1929) is an anatomic consequence and a proof of this intensified activity.

These authors showed that the pressor effect produced in the common carotid artery by stimulation of the central end of the vagus nerve (infrequently observed) or the sciatic nerve is accompanied by a more or less rapid rise in pressure in the mesenteric vein, active contraction of the spleen occurring during this time. In the same manner, when the spleen undergoes active distension in the presence of a depressor effect in the arterial system, the drop in blood pressure in the mesenteric vein is larger than that which occurs when the arterial pressure is reduced with the spleen preliminarily disengaged.

A number of investigations have been devoted to studying the reactions of the spleen in the presence of various emotions. It has been shown that the secretion of adrenilin by the adrenal glands during pain, fright, and anger may cause contraction of the spleen (Cannon, 1927).

It has been established that conditioned reflexes can be induced in splenic activity (K.M. Bykov and M.A. Gorshkov, 1932). The conditioned-reflex arc includes neural and humoral elements. The external stimulus is first transmitted to the cerebral cortex and then along efferent nerves to the adrenals, which secrete adrenilin and ultimately act on the spleen.

It has been established in experiments on animals and observations on humans that the spleen undergoes changes in response to variations in the ambient temperature for local thermal stimulation of the skin (Barcroft, 1926, 1930; V.V. Parin, 1930). The magnitude of the reflex reaction of the spleen depends on the strength of the stimulus (Barcroft, 1930). Heymans (1929) showed that the spleen contracts reflexively when the pressure in the isolated carotid sinus is reduced, while when this pressure is increased the spleen distends. The volume of the spleen decreases in all forms of axphyxia (A.I. Krat, 1958). The extent of the splenic reaction depends on the strength and character of the stimulus applied to the nerve of the carotid sinus (A.P. Polosukhin, 1948).

It follows from these data that the spleen can participate in the body's protective reactions to rather varied environmental factors. The research of A.P. Polosukhin (1948), who conducted experiments on animals of different ages, is quite interesting. Until the age of one and one-half months the spleen of a dog does not actively participate in blood circulation or in the body's protective reactions to various stimuli. Humoral regulation of splenic volume by the adrenals in response to painful stimuli first appears at one and one-half months. Reflex regulation of splenic volume develops at an age of 2-1/2 months or later. Polosukhin assumes that the lack of reflex regulation is associated with the insufficient development of the nervous centers. The underdevelopment of the adrenal cortex is also significant before three weeks of age. "Our data," Polosukhin (1948) concludes, "thus indicate that development of humoral regulatory mechanisms precedes formation of reflex regulation in ontogenesis, just as in phylogenesis."

A.P. Polosukhin's conclusion cannot, however, be regarded as being completely accurate or agreeing with his own experimental results. Judging from his experiments, the point is not that the entire reflex arc to the spleen develops after the adrenals begin to exert their influence, but that that segment of the efferent portion of the reflex arc which passes through the adrenals matures earlier. Thus, more precisely, Polosukhin established that the neurohumoral effector pathway to the spleen matures more rapidly than the purely neural pathway.

The investigations of V.N. Chernigovskiy (1943) were a great stride forward in the study of splenic participation in various bodily processes. Prior to these observations, the spleen had been regarded as almost exclusively an effector organ. Chernigovskiy established that the splenic vascular system is a receptor field that perceives mechanical and chemical stimuli. Various changes in the spleen, serving as stimuli, may cause signals to be dispatched to the central nervous system and result in reflex elevation of arterial pressure, acceleration of heart and respiration rates, and deeper breathing. As Chernigovskiy surmises, there is a flow of impulses from the spleen to the central nervous system, which maintains the tonic excitation of the vasomotor center.

Many attempts have been made to determine the location in the central nervous system of the centers that control the motor activity of the spleen. E.V. Erikson (1900) established that the subcortical center regulating this activity lies in the anterior third of the thalamus opticus. The automatic and reflex centers for the spleen lie between the first and fourth segments of the cervical portion of the spinal cord. Electrical stimulation of this area causes extremely strong splenic contractions. Longitudinal transection of the spinal cord does not eliminate reflex influences on the spleen (I. Bulgak, 1872). It is possible that reflex transmission of impulses to the spleen takes place through the peripheral ganglia (E.V. Erikson, 1900). Bochefontaine (1873-1874), I.R. Tarkhanov (1874), and Roy (1890-1892) observed very slight contractions of the spleen when the myelencephalon was stimulated. N.K. Koryayev (1910) believes that the contraction of the spleen that occurs during asphyxia is due to excitation of nerve centers lying above the third and fourth cervical segments of the spinal cord.

The majority of researchers believe that the reaction of the spleen to asphyxia results from a central rather than a peripheral effect. A.P. Polosukhin (1948) established that the movements of the spleen are regulated by the myelencephalic sympathetic and parasympathetic centers and that denervation of the spleen promotes anemia (Ye. L. Kan, 1954). Surveys of the comparatively recent literature on splenic contractile activity are available in articles by A.P. Polosukhin (1948) and A.S. Dmitriyev (1950), while the literature on humoral influences on the spleen is treated in an article by I.V. Kolpakov (1938).

It has been noted that the solar plexus, which consists of autonomic ganglia of varying size and form, gives rise to a large number of nerve trunks leading to blood vessels that pass near the plexus and to different organs. In addition, these trunks form secondary plexi. The spleen is one of the abdominal organs that receives new trunks from the solar plexus. Here there are approximately the same anatomic relationships between the vessels of the upper abdomen, the solar plexus, and the spleen as between the inferior mesenteric artery, the inferior mesenteric ganglion, and the urinary bladder. This served as grounds for the hypothesis that the solar plexus transmits neural signals regarding local changes in the vascular system to the organs of the upper abdomen, particularly the spleen.

M.A. Vayn-Rib verified this hypothesis experimentally. Several methods have been proposed for studying the motor activity of the spleen. The procedure most widely employed for short-term experiments is N.K. Koryayev's oncographic method, which is based on a suggestion made by N.A. Mislavskiy. As we know, there are various methods for observing splenic motor activity (Barcroft's "celluloid window" in the abdomen, extracutaneous examination of the spleen by Barcroft's method, and x-ray and subcutaneous examination of the spleen by K.M. Bykov's method).

M.A. Vayn-Rib set himself the task of studying the effect on splenic motor activity of changes in pressure in the isolated sinistral gastroepiploic, sinistral gastric, and superior mesenteric arteries and the gastroepiploic and superior mesenteric veins. This experimental setup solved the problem of choosing an observational technique.

N.K. Koryayev's oncographic method was selected. We will not describe this procedure, since it is well-known. The technique by which the blood vessels were isolated has been described in the preceding chapter. We need make only a few brief remarks. The animal was given morphine subcutaneously 40 min before the operation, which was carried out under general anesthesia. In isolating the vessels special care was taken to leave their neural connections intact and to sever all branches leading to the section to be isolated. In different experiments the cannula that served to connect the vessel to the pressure tank was inserted into its central or peripheral end. Only one vessel was isolated at the beginning of the experiment, others being isolated later in accordance with the specific experimental problem. After each experiment the vessel was inspected to make certain that it had been completely isolated.

For this purpose the pressure in the system was raised to 200 mm Hg and the pressure tank was disconnected. If the pressure in the system remained unchanged, the vessel was regarded as having been completely isolated. If the pressure dropped, it was assumed that some branch of the vessel remained intact. Incomplete isolation was encountered in two of 10 cases. We excluded the results of these two experiments from our conclusions. We recorded the blood pressure in one of the common carotid arteries. An interval of 30 min was left between the completion of the disection and the beginning of stimulation.

Figure 12 illustrates the results obtained.

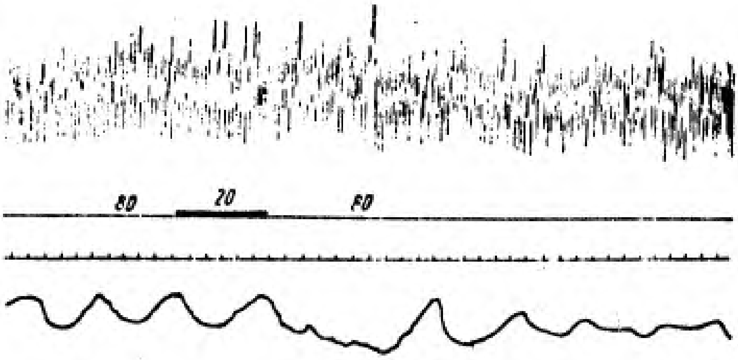


Fig. 12. The upper curve shows the blood pressure in the common carotid artery, the numerals represent the blood pressure in the sinistral gastroepiploic artery, the second curve indicates application of the stimulus, the third curve is a five-second time marker, and the lower curve is an uncometric record of splenic volume.

Fig. 13. The upper curve represents the pressure in the common carotid artery, the second curve is an uncometric record of splenic volume, the numerals indicate the blood pressure in the sinistral gastroepiploic artery, the third curve indicates application of the stimulus, and the lower curve is a 5-sec time marker.

Figure 12 shows data obtained in an experiment conducted on 3 February 1948. The lower curve (see Fig. 12) registers pronounced rhythmic changes in splenic volume. In this experiment we determined the effect of changes in pressure in the isolated gastroepiploic artery. Reducing this pressure from 80 to 20 mm Hg caused a marked decrease in splenic volume. The latent period between the beginning of the pressure change in the isolated artery and the appearance of a noticeable decrease in splenic volume was 27 sec. Raising the pressure in the isolated gastroepiploic artery to its initial level (80 mm Hg) led to restoration of the initial splenic volume, but the rhythmic splenic activity, which had been inhibited by the reduction in pressure in the isolated artery, remained less pronounced than at the beginning of the experiment. There were no marked variations in the blood pressure in the common carotid artery at any point during the experiment; such variations might have resulted from the changes in the isolated sinistral gastroepiploic artery.

The change in splenic volume increased as the variations in pressure in the isolated sinistral gastroepiploic artery became larger (Fig. 13).

Figure 13 shows data obtained in the same experiment as in Fig. 12. These curves indicate that a descending segment of the wave of rhythmic changes in splenic volume developed at the instant when the pressure in the isolated artery was raised from 60 to 180 mm Hg. After 7 sec the descending segment terminated without reaching its minimum and the splenic volume began to increase. [illegible]'s volume was substantially greater after 1 min 40 sec, when the pressure in the isolated arterial segment had risen to 200 mm Hg. It decreased considerably when the pressure in the isolated artery was reduced to zero after 3 min. Again raising the pressure in the isolated artery from 0 to 60 mm Hg caused the splenic volume to increase and to exhibit quite marked rhythmic fluctuations.

The blood pressure in the common carotid artery did not vary noticeably during these observations, except when the pressure in the isolated artery was reduced to zero. The pressure in the carotid artery rose briefly at this point, but the contraction of the spleen was already quite pronounced.

This rise in arterial pressure can consequently be attributed either to an increase in the amount of circulating blood in the vascular system resulting from expulsion of blood by the contracted spleen or to the reflex described by V. N. Chernigovskiy as developing in the spleen when its internal pressure increases. It is quite probable that both factors are important. It was also found that an increase in pressure in the isolated artery was accompanied by an intensification of the rhythmic activity of the spleen, while a decrease in arterial pressure was accompanied by attenuation of this activity.

Figure 14 shows experimental data obtained on 6 February 1948. It illustrates the effect on splenic volume of sharp changes in pressure in the sinistral gastroepiploic artery. Reduction of the arterial pressure from 180 mm Hg to 0 was accompanied by a sharp decrease in splenic volume, the latent period of the reaction being approximately 13 sec. Increasing the pressure in the isolated artery from 0 to 180 mm Hg

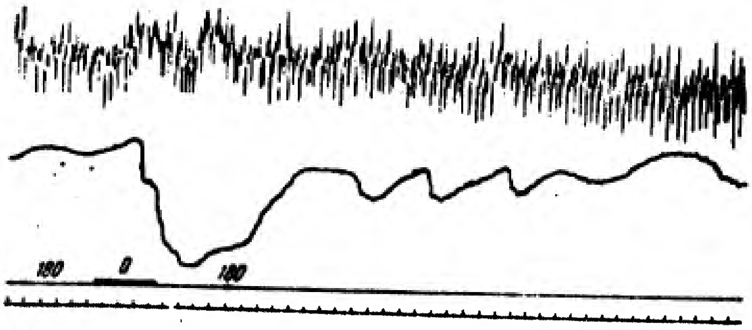


Fig. 14. Curves the same as in Fig. 13.

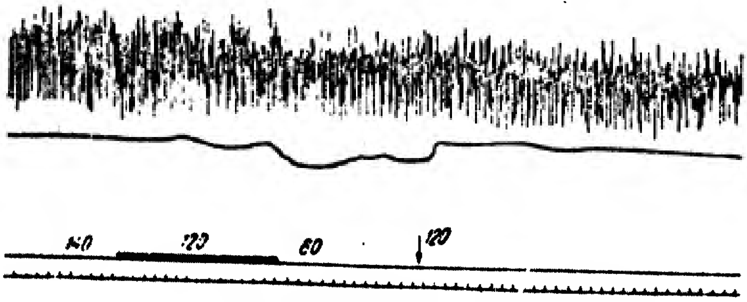


Fig. 15. Curves the same as in Fig. 13.

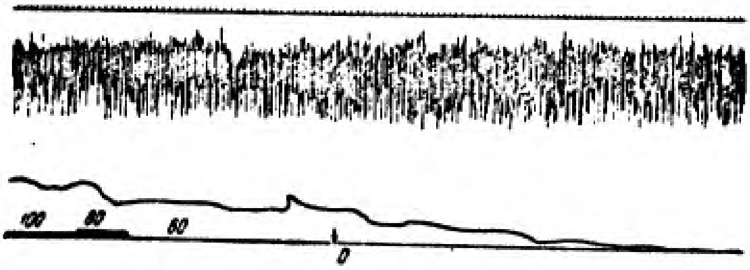


Fig. 16. Curves the same as in Fig. 13.
No time marker.

caused the splenic volume to rise and again exhibit rhythmic fluctuations; the pressure in the common carotid artery did not vary noticeably.

While noting that the most striking changes in splenic volume are produced by substantial pressure variations in the isolated sinistral gastroepiploic artery, we wish to emphasize that changes in splenic volume can also be observed when the pressure fluctuations are comparatively small, e.g., of the order of 20 mm Hg.

Figure 15 illustrates data obtained in an experiment conducted on 24 February 1948. These curves show that a quite marked decrease in splenic volume occurred when the pressure in the isolated sinistral gastroepiploic artery was reduced from 140 to 120 and then to 80 mm Hg. Again raising the pressure in the isolated artery to 120 mm Hg caused the splenic volume to increase.

Figure 16 illustrates the same experiment on 24 February 1948. It can be seen from the curves in Fig. 16 that reducing the pressure in the isolated sinistral gastroepiploic artery from 100 to 80 and then to 60 mm Hg caused a pronounced decrease in splenic volume. Reducing the pressure to zero led to still more severe contraction of the spleen and almost complete cessation of its rhythmic activity. The pressure in the common carotid artery did not undergo any regular changes.

Similar results were obtained when the pressure in the isolated superior mesenteric artery was varied. This is illustrated by Fig. 17 (experiment conducted on 16 February 1948).

It can be seen from the curves in Fig. 17 that an increase in splenic volume occurred when the pressure in the isolated segment of the superior mesenteric artery was raised from 60 to 180 mm Hg. Similar changes in splenic volume were observed in 7 of 10 experiments in which the pressure in the sinistral gastroepiploic and superior mesen-

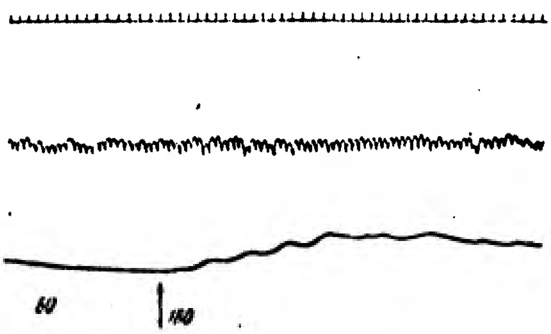


Fig. 17. The upper curve is a 5-sec time marker, the second curve represents the pressure in the common carotid artery, and the third curve is an uncometric record of splenic volume. The numerals beneath the lower curve indicate the pressure in the superior mesenteric artery.

teric arteries was varied. The latent period of the reaction ranged from 7 to 35 sec.

Observation of the changes in splenic volume when the pressure in the isolated sinistral gastric artery and the gastroepiploic and superior mesenteric veins was varied did not yield positive results. Since the spleen may react to changes in pressure in the isolated sinistral gastroepiploic and superior mesenteric arteries against a background of constant pressure in the common carotid artery and unaltered respiration, it can be assumed that the reactive signal pathways from the arterial receptors to the spleen may run not through the central nervous system but through the solar plexus, forming peripheral reflex arcs in its ganglia.

The validity of this hypothesis was demonstrated by the following series of experiments. In one experiment the subject's spinal cord was severed immediately below the medulla (Fig. 18).

After transection of the spinal cord the pressure in the common carotid artery dropped sharply, the spleen contracted strongly, and the rhythmic fluctuations in its volume ceased. Both vagal sympathetic trunks were transected in the cervical region and 40 ml of warm physio-

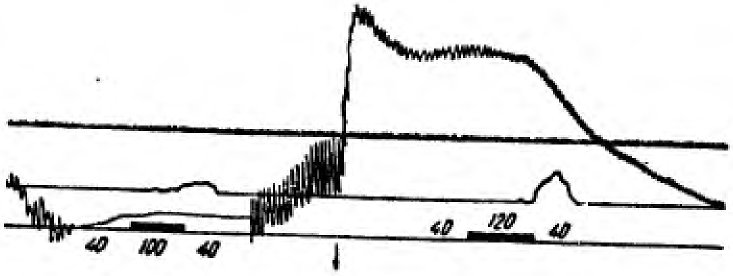


Fig. 18. Curves the same as in Fig. 17. The lower curve indicates application of the stimulus.

logical solution was injected into the external jugular vein. The pressure in the common carotid artery rose substantially at first, but soon began to drop. While the pressure in the common carotid artery was falling, the pressure in the isolated sinistral gastroepiploic artery was raised from 40 to 120 mm Hg, so that, despite the continuing decrease in general arterial pressure, the spleen increased in volume. Artificial respiration was discontinued when the pressure in the common carotid artery had fallen to 15 mm Hg, i.e., several tests to determine the effect of increased pressure in the isolated sinistral gastroepiploic artery were made against a background of asphyxia (Fig. 19).

The curves in Fig. 19 clearly show that, despite the low general arterial pressure, the spleen responded to each rise in pressure in the isolated artery with an increase in volume, while the pressure in the common carotid artery remained unchanged. The results of this experiment are very important for analyzing local reflex pathways. First of all, we were able to observe an increase in splenic volume under the influence of local stimulation of an isolated artery against a background of very low general arterial pressure after artificial respiration had been halted, i.e., when the central influences on the spleen were a strong stimulus to contraction. Secondly, the spleen responded with an increase in volume to local stimulation of the isolated artery while the general arterial pressure was dropping, i.e., when the central stimuli called for a reduction in volume.

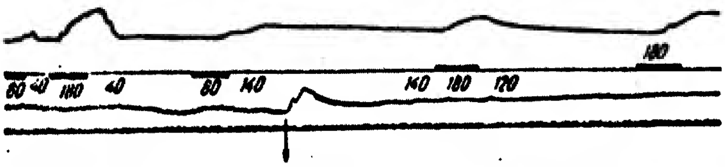


Fig. 19. The upper curve is an uncometric record of splenic volume, the second curve indicates application of the stimulus, the numerals represent the blood pressure in the sinistral gastroepiploic artery, the third curve shows the pressure in the common carotid artery, and the lower curve is a one-second time marker.

Similar results were obtained in several other experiments. The results of recent observations have completely confirmed the hypothesis that reflex signals may be transmitted from the receptors of the abdominal vessels to the spleen through the ganglia of the solar plexus.

One objection to this conclusion is the fact that the spinal cord was not destroyed in our experiments. Reflex transmission to the spleen from the receptors of the abdominal vessels must consequently still have been possible. Even more serious consideration must be given this factor as a result of the fact that there are data indicating that the "automatic and reflex" center for the spleen lies between the 1st and 4th cervical segments of the spinal cord (I. Bulgak, 1872).

There are two reasons why this objection cannot be considered convincing. First, the conclusion that the spinal center for the spleen is located in the cervical region cannot be regarded as proved, since it has been disputed by a number of authors (A.P. Polosukhin, 1948; et al.) whose research was subsequent to that of I. Bulgak and who asserted that this center lies in the myelencephalon. The hypothesis that the nerve center for the spleen is located in the spinal cord seems dubious since it is based on observation of splenic contractions during electrical stimulation of the cervical portion of the cord. Such stimulation should alter the state of the spleen both by exciting the nerve centers and by exciting the tract linking the myelencephalon to the periphery, including the spleen.

Secondly, even if there actually were a "nerve center for the spleen" in the cervical portion of the spinal cord, the shock produced by separation of the spinal cord from the myelencephalon would inevitably halt its activity, just as the activity of the spinal segmental vasomotor centers inevitably stops for quite some time under such conditions. The physiological properties of the so-called spinal splenic nerve center can in no way differ from those of the segmental vasomotor centers.

We induced a splenic reaction by varying the pressure in isolated abdominal arteries against a background of sharply reduced blood pressure, i.e., when the spinal vasomotor centers were disengaged. This enables us to affirm that the splenic reaction analyzed was effected by peripheral reflex arcs.

What is the physiological significance of these facts?

The structural characteristics of the spleen have long forced us to assume that it plays an active part in creating the optimum blood-pressure level, expelling blood when the amount in the vascular system decreases and taking in blood when there is an "excess" in the vascular system. The many important investigations conducted to elucidate this mechanism have failed to determine the character of the "actuating" mechanism that causes the spleen to begin functioning to equilibrate fluctuations in blood pressure. They have produced only the supposition that the actuating mechanism lies in the central nervous system and is common to the entire vascular system.

As a result of the discovery of vascular receptor fields that can obviously induce enlargement and contraction of the spleen, it has become clear that, in addition to the central mechanism common to the entire vascular system, there is a "local" actuating mechanism for active participation of the spleen in creating an optimum pressure level in the abdominal vessels. We have therefore designated vascular receptor fields of this type as "local" without denying the possibility that they may give rise to general reflex reactions (general changes in the state of the vascular system, respiration, muscular activity, etc.). An increase in pressure in these vessels automatically induces distension of the spleen by local transmission through the neurons of the solar plexus; a drop in pressure may automatically evoke a decrease in the volume of the spleen by stimulating its contractile activity. In both cases the ultimate effect is to equilibrate the blood pressure in the abdominal vessels and maintain its optimum level. These vessels have an extremely large possible capacity. The existence of a local mechanism that regulates splenic volume in accordance with the pressure in the abdominal vessels undoubtedly has a favorable effect on cardiac activity and on the blood supply to all organs, particularly those of the abdomen.

This explains the importance of the factors described above in circulatory physiology and pathology. Since the stimuli employed in our experiments were adequate to stimulate sensory but not motor endings, we naturally must have excluded the possibility that these reactions could be effected by the axon-reflex mechanism of the efferent sympathetic fibers. They were therefore carried out by peripheral, or local reflexes.

Chapter 6

REFLEXES FROM THE ABDOMINAL VESSELS TO THE KIDNEYS

An experimental study of the reflex influences exerted on renal activity by the abdominal vessels was conducted in our laboratory by L.A. Toporkova. Renal activity is regulated by a very complex mechanism incorporating neural and humoral components. The parasympathetic and sympathetic systems provide the effector innervation of the kidneys. The vagus nerve provides renal parasympathetic innervation. The renal sympathetic fibers rise from the spinal cord between the 6th thoracic and 2nd lumbar segments and are discontinuous in the sympathetic ganglia of the solar plexus, through which the vagal fibers also pass; they are then incorporated into the greater and lesser splanchnic nerves of the sympathetic trunk and, together with the vagal fibers, into the renal plexus. Nerve fibers from the renal plexus enter the renal tissue as concomitants of blood vessels, all the elements of this tissue (the tubules, the incoming and outgoing vessels of the glomeruli, etc.) being richly supplied with their endings. It is customarily assumed that the afferent fibers originating in the kidneys have their somae in the spinal ganglia and are incorporated into the lesser splanchnic nerve.

V. Smirnov (1901) described the histological characteristics of renal innervation. A monograph by B.D. Kravchinskiy (1949) presents the results of physiological investigations of various aspects of renal activity conducted by L.A. Orbeli's students. A number of investigations have been devoted to the functional interactions between the kidneys and other urinary organs and between the kidneys and other abdominal organs. In particular, Z.V. Bebeshina and G.P. Konradi (1934) showed that an increase in bladder pressure for injection of resorcine or collargol into the bladder inhibits renal activity.

Interesting data on the characteristics of the reflex relationships between the kidneys and other elements of the urinary apparatus and between the kidneys and organs of other physiological systems have been presented by G.M. Shpuga and her colleagues (G.M. Shpuga, 1947; A.A. Lebedev, 1955; G.M. Shpuga and A.A. Lebedev, 1957; N.A. Myasoyedova, 1957; G.D. Anikin, A.A. Lebedev, Ye.I. Tyurin, and S.A. Yaroslavtsev, 1957; et al.).

In our opinion, of particular interest in this research are the results of observations on the restoration of sensory innervation in the transplanted kidney. Experimental induction of renal colic in an intact kidney causes severe inhibition of uropoiesis in the other kidney, sometimes to the point of complete arrest; the periodic motor activity and evacuatory and secretory functions of the empty stomach are altered.

N.A. Myasoyedova (1948, 1950, 1952, 1958, et al.) points out that the character of the renal reflex reactions to stimulation of the mechanoreceptors and chemoreceptors of the alimentary tract depends on the functional state of the central nervous system. The following facts, which she established, merit serious attention:

1) transection of the vagus nerves below the diaphragm does not eliminate the reflex influences exerted by the stomach on the kidneys;

2) disruption of the integrity of the sympathetic trunks in the lumbar region does not prevent transmission of reflexes from the rectum to the kidneys;

3) reflexes from the stomach and cecum to the kidneys are not

eliminated by transection of the spinal cord at the level of the 1st lumbar vertebra. These reflexes can be eliminated by also transecting the sympathetic trunks in the pelvic and lumbar regions. In S.Ya. Yaroslavtsev's opinion (1957), there are viscerovisceral reflexes between the permatic cords and the kidneys.

Renal activity can be modified by stimulating the interoceptors of the lungs and pleura (R.O. Faytel'berg and S.O. Ochan, 1953; D.A. Kocherga, 1953). All the data presently available on changes in renal activity indicate that the reflex pathways to the kidneys are quite complex and may pass through the peripheral sympathetic ganglia. Reflex reactions may take place in the kidneys even when the corresponding spinal centers are disengaged.

L.A. Toporkova conducted 24 experiments on dogs to study the effect of variations in pressure in isolated arteries (the superior and inferior mesenteric and sinistral gastroepiploic arteries) on uropoiesis in both kidneys. During the preparations for the experiment (opening of the abdomen, location and isolation of the requisite blood vessels, insertion of cannulas into the ureters, etc.) the animals were kept under morphine and ether-chloroform anesthesia. Glass cannulas were inserted into both ureters and their ends were placed over glass beakers, so that the drops of urine excreted from both kidneys could be collected and counted. The number of drops of urine produced per minute was calculated throughout the entire experiment. The arteries were isolated simultaneously or sequentially, depending on the purpose of the investigation. The isolation procedure was described in previous chapters.

The receptors were stimulated by varying the pressure in the isolated vessels; the change in pressure was either "constant" or "pulsating." A "constant" increase in pressure in an isolated artery was maintained for different periods, 5-10 min in the majority of cases, and the pressure was then reduced to zero for an equal time. The pressure was raised to 90-100-120-140-160 mm Hg. The pulsating-pressure amplitude ranged from 0-70-100 to 100-140-160 mm Hg.

Three series of experiments were conducted. In the first series Toporkova studied the effect of changes in pressure in the isolated arteries on uropoiesis before transection of the spinal cord below the myelencephalon; in the second series she determined the effect of the same stimuli before and after transection of the spinal cord; in the third series she studied the effect of the same stimuli before and after complete removal of the thoracic, lumbar, and sacral segments of the spinal cord.

After transection or partial or complete removal of the spinal cord the blood pressure in the common carotid artery dropped sharply, to 20-40 mm Hg. Uropoiesis was completely arrested during this period. The animal was given artificial respiration. The pressure in the common carotid artery gradually rose to 60-90 mm Hg, this requiring from 40 min to 2 hr. The rise in pressure was accompanied by a gradual restoration of urine production. In order to accelerate the restoration of this process, 200-400 ml (depending on the animal's weight) of physiological solution heated to 37-38° was injected into the blood stream, usually through the external jugular vein, thus reducing the protein pressure of the blood. This promoted an intensification of filtration processes, including uropoiesis, and a slight acceleration of the rise in arterial pressure.

Table 4 presents the results obtained in the first series of experiments.

Summarizing the results of the seven experiments shown in Table 4, we can state that a nonfluctuating (constant) rise in pressure in the

TABLE 4

1 Дата проведения опыта	2 Продолжительность наблюдения (в минутах)	3 Название артерии	4 Давление (в мм рт. ст.)	5 Количество капель мочи, выделенных			
				6 правой почкой		9 левой почкой	
				7 до раздражения артерии	8 во время раздражения артерии	7 до раздражения артерии	8 во время раздражения артерии
12/I 1949 г. (вес животного 4,47 кг) 10	7	13 Верхняя брыжеечная	160	3	7	0	3
	8	Она же пульсирующая 14	0—140	5	3	3	2
	8	Нижняя брыжечная	140	3	4	2	4
	10	Она же пульсирующая 14 15	0—140	4	3	3	2
	10	То же 16	0—140	2	—	2	—
13/I 1949 г. (вес животного 11 кг) 11	8	13 Верхняя брыжеечная	160	11	15	12	18
	8	Она же пульсирующая 14 15	0—140	12	13	12	12
	10	Нижняя брыжеечная	160	15	22	16	24
	10	Она же пульсирующая 14	0—140	15	13	14	15
	10	То же 16	0—140	13	—	15	—
15/I 1949 г. (вес животного 13 кг) 12	10	13 Верхняя брыжеечная	160	32	37	27	45
	10	Она же пульсирующая 14 15	160	28	29	28	32
	10	Нижняя брыжеечная	160	23	29	20	30
	8	Она же пульсирующая 14	0—140	13	12	16	14
	8	Левая желудочно-сальниковая 17	160	10	10	12	13
	8	Она же пульсирующая 14	0—160	8	9	11	10
17/I 1949 г. (вес животного 9 кг) 18	10	13 Верхняя брыжеечная	160	20	30	17	35
	10	Она же пульсирующая 14 15	160	20	23	15	16
	10	Нижняя брыжеечная	160	20	25	15	21
	8	Она же пульсирующая 14	0—160	16	12	12	15
	10	Левая желудочно-сальниковая 17	160	20	20	15	20
	10	Она же пульсирующая 14	0—160	16	16	12	12
25/I 1949 г. (вес животного 9,4 кг) 19	10	13 Верхняя брыжеечная	160	95	117	58	84
	10	Она же пульсирующая 14 15	100—160	97	95	60	74
	10	Нижняя брыжеечная	160	93	111	68	87
	10	Она же пульсирующая 14	100—160	99	100	71	72
	10	Левая желудочно-сальниковая 17	160	91	94	70	76
	10	Она же пульсирующая 14	100—160	91	86	61	61
7/II 1949 г. (вес животного 6,2 кг) 20	10	13 Верхняя брыжеечная	160	155	178	140	175
	10	Она же пульсирующая 14 15	100—160	158	168	143	160
	10	Нижняя брыжеечная	160	166	176	141	158
	10	Она же пульсирующая 14	100—160	160	160	141	148
	10	Левая желудочно-сальниковая 17	160	150	161	142	149
	10	Она же пульсирующая	100—160	148	150	144	140

TABLE 4 (continued)

Дата проведения опыта 1	Продолжительность наблюдения (в минутах) 2	Название артерии 3	Давление (в мм рт. ст.) 4	Количество капель мочи, выделенных 5 правой почкой 6 до раздражения артерии 7	правой почкой 6 во время раздражения артерии 8	левой почкой 9 до раздражения артерии 7	левой почкой 9 во время раздражения артерии 8
15/II 1949 г. 21	10	Верхняя брыжеечная 13	160	205	216	89	100
	10	Она же пульсирующая 14	100–160	201	218	98	104
	10	Нижняя брыжеечная 15	160	210	232	100	115
	10	Она же пульсирующая 14	100–160	212	217	100	99
	10	Левая желудочно-сальниковая 17	160	192	200	100	106
	10	Она же пульсирующая 14	100–160	191	183	100	101

1) Date of experiment; 2) observation time (in min); 3) artery; 4) pressure (in mm Hg); 5) number of drops of urine excreted; 6) right kidney; 7) before stimulation of artery; 8) during stimulation of artery; 9) left kidney; 10) 12 January 1949 (animal weighing 4.47 kg), 11) 13 January 1949 (animal weighing 11 kg); 12) 15 January 1949 (animal weighing 13 kg); 13) superior mesenteric; 14) the same, pulsating; 15) inferior mesenteric; 16) the same; 17) sinistral gastroepiploic; 18) 17 January 1949 (animal weighing 9 kg); 19) 25 January 1949 (animal weighing 9.4 kg); 20) 7 February 1949 (animal weighing 6.2 kg); 21) 15 February 1949.

isolated superior and inferior mesenteric arteries stimulates uropoiesis in both kidneys. This mechanism is quite clearly manifested in those experiments in which uropoiesis was initially profuse (experiments of 25 January, 7 February, and 15 February). In the latter two experiments physiological solution, 25% saline solution, gelatin, and urea were preliminarily injected into the animal's blood stream. It can be assumed that the copious uropoiesis in these animals was due to administration of these solutions, the majority of which are diuretics. It is quite possible that diuretics increase renal sensitivity to subsequent stimulation from the vascular receptor fields. There was no material difference in the effects produced by raising the pressure in the superior and inferior mesenteric arteries. A more pronounced reaction was sometimes produced by an increase in pressure in the superior mesenteric artery (experiment of 13 January) and sometimes by a rise in pressure in the inferior mesenteric artery (experiment of 12 January). Raising the pressure in the sinistral gastroepiploic artery had the least effect in all cases, actually producing no reaction in the experiments of 15 January and 17 January 1949.

Two pulsating-pressure variants were employed, from 0 to 100 mm and from 100 to 160 mm Hg. In both instances use of "pulsating" pressure yielded the least definite results. In some experiments (e.g., that of 13 January) a pulsating rise in pressure in the superior and inferior mesenteric arteries had no effect whatsoever on uropoiesis. In other experiments (that of 12 January) a pulsating increase in pressure in the superior and inferior mesenteric and sinistral gastroepiploic arteries caused an intensification of uropoiesis in one kidney and simultaneously inhibited or did not affect uropoiesis in the other kidney. In four experiments a pulsating rise in pressure produced an intensification of uropoiesis, but the extent of the increase was substantially less than in those experiments involving a constant rise in pressure.

The indeterminacy of the effect of "pulsating" rises in pressure was not unexpected, since substantial brief increases and decreases in pressure (within the range 0-140 or 0-160 mm) act differently on the receptors, to some extent neutralizing one another, this being manifested in the variability and attenuation of the renal reactions.

A pulsating increase in pressure between 100 and 160 mm Hg was somewhat more effective. This to a large extent confirms the hypothesis that the effect of a variation in pressure becomes more pronounced as the difference between the maximum and minimum pressures decreases.

Adaptation to the action of increased pressure in isolated arteries is very slow. This conclusion is based on protracted observation of uropoiesis. At times no adaptation could be detected throughout the entire 10-min action of the elevated pressure.

In the next series of experiments the effects of changes in pressure in isolated arteries were determined before and after transection of the spinal cord (Table 5).

The results of the second series of experiments confirm the data obtained in the first series of observations. Moreover, they establish that transection of the spinal cord below the myelencephalon does not eliminate the stimulatory effect of elevated pressure in the isolated superior and inferior mesenteric and sinistral gastroepiploic arteries on uropoiesis. Stimulation of the sinistral gastroepiploic artery had the weakest effect.

In order to be able to observe the action of elevated pressure in isolated arteries on renal uropoietic activity after transection of the spinal cord below the myelencephalon, one must apply artificial respiration and wait for the arterial pressure in the systemic circu-

TABLE 5

1 Дата проведения опыта	2 Продолжительность наблюдения (в минутах)	3 Название артерии	4 Высота давления (в мм рт. ст.)	5 Количество капель мочи, выделенных: 6 правой почкой: 7 до раздражения артерии	8 во время раздражения артерии	9 левой почкой: 7 до раздражения артерии	8 во время раздражения артерии
10 26/XII 1949 г.	5	Нижняя брыжеечная 13	120	12	15	0	0
	5	» »	140	11	14	0	0
	5	Она же пульсирующая 14	0—140	11	15	0	0
		15 Спинной мозг перерезан под продолговатым мозгом. Кровяное давление понизилось до 20—24 мм рт. ст. Отделение мочи прекратилось. Применялось искусственное дыхание. Через 45 минут кровяное давление повысилось до 60 мм рт. ст.					
11 28/XII 1949 г.	5	Нижняя брыжеечная	120	5	8	0	0
	5	Верхняя 13 »	120	8	11	0	0
	10	» 16 »	140	15	20	5	9
		17 Произведена перерезка мозга под продолговатым. Кровяное давление упало с 75—78 до 25 мм рт. ст. Применялось искусственное дыхание. Через 1 час 10 минут давление поднялось до 42 мм рт. ст.					
12 3/I 1950 г. (вес животного 7 кг)	5	Верхняя брыжеечная	120	4	5	2	2
	5	» » 16	140	2	2	0	0
	5	» »	120	13	18	18	22
	5	Нижняя 13 »	120	15	19	15	21
	5	Верхняя 16 »	140	16	21	14	19
	5	Верхняя брыжеечная	140	7	9	8	14
		18 Мозг перерезан под продолговатым. Кровяное давление упало с 95—98 до 32 мм. рт. ст. Применялось искусственное дыхание. Через 1 час 10 минут давление поднялось несколько выше 60 мм рт. ст.					

1 Дата проведения опыта	2 Продолжительность наблюдений (в минутах)	3 Название артерии	4 Высота давления (в мм рт. ст.)	5 Количество капель мочи, выделенных: 6 правой почкой: 7 до раздражения артерии	8 во время раздражения артерии	9 левой почкой: 7 до раздражения артерии	8 во время раздражения артерии
19 6/I 1950 г. (вес животного 12 кг)	5	Нижняя 13 »	140	4	6	7	6
	5	Верхняя 16 »	120	16	24	13	26
	5	» »	140	16	25	17	20
	5	Нижняя »	120	15	29	16	30
	5	» »	140	16	30	16	25
		21 Мозг перерезан под продолговатым. Артериальное давление упало с 99—101 до 38 мм рт. ст. Производилось искусственное дыхание. Через 1 час 30 минут давление 65—67 мм рт. ст.					
20 20/I 1950 г. (вес животного 21,7 кг)	5	Верхняя брыжеечная	120	7	19	12	15
	5	» 16 »	140	14	19	14	15
	5	Нижняя »	120	15	19	11	14
	5	» 13 »	140	12	11	10	10
	5	Верхняя »	120	22	25	36	42
	5	» »	140	23	29	37	43
	5	Нижняя »	120	23	28	40	48
	5	» »	140	25	34	38	49
	5	Левая желудочно-сальниковая 22	120	26	30	36	38
	5	То же 23	140	27	31	35	34
		24 Мозг перерезан под продолговатым. Артериальное давление упало со 125—128 до 25 мм рт. ст. Применялось искусственное дыхание. Через 48 минут давление поднялось до 60 мм рт. ст.					

TABLE 5 (continued)

1 Дата проведения опыта	2 Продолжительность наблюдения (в минутах)	3 Название артерии	4 Высота давления (в мм рт. ст.)	5 Количество капель мочи, выделенных			
				6 правой почкой		9 левой почкой	
				7 до раздражения артерии	8 во время раздражения артерии	7 до раздражения артерии	8 во время раздражения артерии
20/I 1950 г. 25	5	16 Верхняя брыжеечная	120	3	4	6	8
	5	» »	140	3	5	4	8
	5	Нижняя 13 »	140	3	4	4	7
	5	Левая желудочно-сальниковая	120	4	4	1	1
		.22 16					
	5	Верхняя брыжеечная	120	23	26	19	31
	5	» »	140	19	23	19	27
	5	Нижняя »	120	15	17	20	24
	5	» 13 »	140	15	21	17	21
	5	Левая желудочно-сальниковая 22	140	16	19	19	22
	5	То же	140	16	16	16	11
		27 Мозг перерезан под продолговатым. Артериальное давление упало со 125 до 30 мм рт. ст. Применялось искусственное дыхание. Введено 400 мл физиологического раствора. Через 1 час 10 минут давление поднялось до 38 мм рт. ст. Снова введено 200 мл физиологического раствора.					
26/I 1950 г. 26	5	16 Верхняя брыжеечная	140	8	10	5	9
	5	Нижняя 13 »	140	5	11	5	9
	5	Левая желудочно-сальниковая 22	140	5	6	4	8
	5	Верхняя брыжеечная	140	3	7	4	8
	5	Нижняя »	140	1	2	3	4

1) Date of experiment; 2) observation time (in min); 3) artery; 4) pressure (in mm Hg); 5) number of drops of urine excreted; 6) right kidney; 7) before stimulation of artery; 8) during stimulation of artery; 9) left kidney; 10) 26 December 1949; 11) 28 December 1949; 12) 3 January 1950 (animal weighing 7 kg); 13) inferior mesenteric; 14) the same, pulsating; 15) spinal cord transected below myelencephalon. Blood pressure dropped to 20-24 mm Hg. Uropoiesis ceased. Artificial respiration was applied. Blood pressure rose to 60 mm Hg after 45 min; 16) superior mesenteric; 17) spinal cord transected below myelencephalon. Blood pressure dropped from 75-78 to 25 mm Hg. Artificial respiration was applied. Blood pressure rose to 42 mm Hg after 1 hr 10 min; 18) spinal cord transected below myelencephalon. Blood pressure dropped from 95-98 to 32 mm Hg. Artificial respiration was applied. Blood pressure rose to slightly above 60 mm Hg after 1 hr 10 min; 19) 6 January 1950 (animal weighing 12 kg); 20) 20 January 1950 (animal weighing 21.7 kg); 21) spinal cord transected below myelencephalon. Arterial pressure dropped from 99-101 to 38 mm Hg. Artificial respiration was applied. Blood pressure rose to 65-67 mm Hg after 1 hr 30 min; 22) sinistral gastroepiploic; 23) the same; 24) spinal cord transected below myelencephalon. Arterial pressure dropped from 125-128 to 25 mm Hg. Artificial respiration was applied. Blood pressure rose to 60 mm Hg after 48 min; 25) 20 January 1950; 26) 26 January 1950; 27) spinal cord transected below myelencephalon. Arterial pressure dropped from 125 to 30 mm Hg. Artificial respiration was applied. A total of 400 ml of physiological solution was administered. Blood pressure rose to 38 mm Hg after 1 hr 10 min. An additional 200 ml of physiological solution was administered.

latory system to rise to the level necessary for restoration of filtration processes. In our experiments this required from 40 min to 2 hr (an average of more than 1 hr). Uropoiesis never reached the same level after restoration as before transection of the spinal cord. This is quite understandable, since the arterial pressure did not revert to its initial level.

This must be taken into account in deciding whether or not increased pressure in the isolated arteries has a stimulatory effect on uropoiesis after separation of the spinal cord from the myelencephalon. If we consider only the absolute increase in the number of drops of urine produced when the pressure in the isolated arteries was raised, this increase is, in the overwhelming majority of cases, less than in similar observations made before the spinal cord was transected. However, this cannot serve as irrefutable grounds for concluding that the effect of the stimulus was attenuated, since many of the conditions affecting uropoietic activity were altered by transection of the spinal cord. A decrease in arterial pressure in the systemic circulatory system sharply reduces uropoiesis. Consideration must be given to the fact that the increase in uropoiesis during the rise in pressure in the isolated arteries drops in a manner that is in no way proportional to the decrease in the total amount of urine excreted after the spinal cord is transected. Moreover, in individual cases these values may be almost the same as before transection of the cord. Thus, the comparative values (the total decrease in the amount of urine produced and the attenuation of the rise in uropoiesis during stimulation) create the impression that, as soon as automatic uropoiesis sets in after separation of the myelencephalon from the spinal cord, a rise in pressure in the isolated superior and inferior mesenteric arteries stimulates urine production to a greater extent than before transection of the spinal cord.

We determined the effect of raising arterial pressure from 0 to 120 mm and from 0 to 140 mm Hg. It was found that the strongest stimulus did not always have the most pronounced effect. Raising the pressure to 120 mm Hg often had a stronger effect than raising it to 140 mm Hg. Similar data were also obtained in the first series of experiments. Correct interpretation of the final results thus requires consideration of both the stimulus strength and a number of other factors, particularly the functional variability of the effector organ under the influence of other factors acting in the body during the observation period.

In the third series of experiments we studied the effect of variations in pressure in the isolated arteries before and after partial or complete destruction of the spinal cord and transection of both vagal sympathetic trunks in the cervical region. Table 6 presents the results of these observations.

The data obtained in the third series of experiments expand the results of our prior observations. These experiments establish that partial or complete destruction of the spinal cord and transection of both vagal sympathetic trunks in the cervical region do not attenuate the stimulatory effect on uropoiesis of elevated pressure in the isolated inferior and superior mesenteric arteries. We were able to make certain that, after destruction of the uropoiesis-regulating spinal centers, the blood pressure in the systemic circulatory system rose to the level necessary for filtration processes, particularly urine production. An increase in pressure in the isolated superior and inferior mesenteric arteries can stimulate uropoiesis both before and after disengagement of the central nervous system. Such stimulation can take place without a prior or parallel rise in blood pressure in the systemic circulatory system.

TABLE 6

1 Дата проведения опыта	2 Продолжительность наблюдений (в минутах)	3 Название артерии	4 Высота давления (в мм рт. ст.)	5 Количество капель мочи, выделенной			
				6 правой почкой		9 левой почкой	
				7 до раздражения артерии	8 но время раздражения артерии	7 до раздражения артерии	8 во время раздражения артерии
20/II 1950 г. (вес животного 8 кг) 10	8	Верхняя брыжеечная 13	140	37	44	13	17
	8	Нижняя 14 »	140	31	40	15	20
		15 Из нижней части грудной и пояснично-крестцовой области удален спинной мозг. Кровяное давление в общей сонной артерии 13 упало со 140 до 80—90 мм рт. ст.					
29/III 1950 г. (вес животного 12 кг) 11	5	Верхняя брыжеечная	140	5	8	4	7
	5	Нижняя »	140	5	8	6	10
	5	Верхняя 14 »	160	10	13	10	11
	5	Нижняя »	160	10	12	10	10
		16 Спинной мозг удален от III—IV сегмента грудной области до конца. У животного самостоятельное дыхание. Давление в общей сонной артерии упало со 120—130 до 68—72 мм рт. ст. Мочеотделение резко уменьшилось. Введено 300 мл физиологического раствора. Мочеотделение увеличилось.					
31/III 1950 г. (вес животного 21 кг) 12	5	Верхняя брыжеечная	160	13	12	10	15
	5	Нижняя »	160	9	9	7	8
	5	Верхняя 13 »	160	23	29	25	31
	5	Нижняя 14 »	160	25	27	21	30
	5	Левая желудочно-17 сальниковая	160	25	24	28	26
		18 Спинной мозг удален в грудном, поясничном и крестцовом отделах. Сохранилось диафрагмальное дыхание. Кровяное давление в общей сонной артерии упало со 140—150 до 40—50 мм рт. ст. Через 1 час 10 минут поднялось до 80—90 мм рт. ст. В наружную яремную вену введено 400 мл физиологического раствора.					

1 Дата проведения опыта	2 Продолжительность наблюдений (в минутах)	3 Название артерии	4 Высота давления (в мм рт. ст.)	5 Количество капель мочи, выделенной			
				6 правой почкой		9 левой почкой	
				7 до раздражения артерии	8 во время раздражения артерии	7 до раздражения артерии	8 во время раздражения артерии
14/IV 1950 г. (вес животного 11 кг) 31/III 1950 г. 19	5	17 Левая желудочно-сальниковая	160	16	15	14	14
	5	Верхняя брыжеечная 13	160	15	17	11	14
	5	Нижняя 14 »	160	15	18	10	15
	5	Верхняя »	160	26	30	15	23
	5	Нижняя »	160	26	30	19	25
		22 Удален спинной мозг в грудном, поясничном и крестцовом отделах. Дыхание диафрагмальное. Артериальное давление упало со 125—130 до 20—40 мм рт. ст. Введено 350 мл физиологического раствора. Через 1 час 40 минут давление в сонной артерии поднялось до 60—58 мм рт. ст.					
26/IV 1950 г. (вес животного 11 кг) 20	10	Верхняя брыжеечная	160	4	6	5	6
	5	Нижняя 14 » 13	160	4	5	5	5
	10	Верхняя »	160	29	34	20	26
	10	Нижняя »	160	28	31	22	29
		23 Спинной мозг удален полностью. Искусственное дыхание. Артериальное давление упало со 130—140 до 30—35 мм рт. ст. Введено в наружную яремную вену 400 мл физиологического раствора. Через 45 минут давление в сонной артерии поднялось до 70—75 мм рт. ст. и возобновилось мочеотделение.					
9/V 1950 г. (вес животного 8,2 кг) 21	10	Верхняя брыжеечная	160	13	17	8	15
	10	Нижняя 14 » 13	160	11	17	12	15
	10	Верхняя брыжеечная пульсирующая 24	70—160	7	10	9	13
	10	Нижняя брыжеечная	70—160	6	10	6	9
	5	Верхняя »	160	26	32	25	30
	5	Нижняя »	160	25	30	21	27

TABLE 6 (continued)

Дата проведения опыта 1	Продолжительность наблюдений (в минутах) 2	Название артерии 3	Высота давления (в мм рт. ст.) 4	Количество капель мочи, выделенной 5			
				правой почкой 6		левой почкой 9	
				до раздражения артерии 7	во время раздражения артерии 8	до раздражения артерии 7	во время раздражения артерии 8
		25 Спинной мозг удален полностью. Искусственное дыхание. На шее перерезаны оба ваго-симпатических нерва. Давление в сонной артерии упало со 130—140 до 20—30 мм рт. ст. Мочеотделение прекратилось. Введено 400 мл физиологического раствора. Через 50 минут кровяное давление поднялось до 70—75 мм. Мочеотделение возобновилось.					
	5	13 Верхняя брыжеечная	160	8	9	5	7
	5	Нижняя » 14	160	6	7	3	5

1) Date of experiment; 2) observation time (in min); 3) artery; 4) pressure (in mm Hg); 5) number of drops of urine excreted; 6) right kidney; 7) before stimulation of artery; 8) during stimulation of artery; 9) left kidney; 10) 20 February 1950 (animal weighing 8 kg); 11) 29 March 1950 (animal weighing 12 kg); 12) 31 March 1950 (animal weighing 21 kg); 13) superior mesenteric; 14) inferior mesenteric; 15) spinal cord removed from lower thoracic and lumbo-sacral regions. Blood pressure in common carotid artery dropped from 140 to 80-90 mm Hg; 16) spinal cord removed from 3rd-4th thoracic segment down. Animal maintained spontaneous respiration. Pressure in common carotid artery dropped from 120-130 to 68-72 mm Hg. Uropoiesis severely reduced. A total of 300 ml of physiological solution was administered. Uropoiesis increased; 17) sinistral gastroepiploic; 18) spinal cord removed in thoracic, lumbar, and sacral regions. Diaphragmal respiration maintained. Blood pressure in common carotid artery dropped from 140-150 to 40-50 mm Hg. Pressure rose to 80-90 mm Hg after 1 hr 10 min. A total of 400 ml of physiological solution was injected into the external jugular vein; 19) 14 April 1950 (animal weighing 11 kg), 31 March 1950; 20) 26 April 1950 (animal weighing 11 kg); 21) 9 May 1950 (animal weighing 8.2 kg); 22) spinal cord removed in thoracic, lumbar, and sacral regions. Diaphragmal respiration maintained. Arterial pressure dropped from 125-130 to 20-40 mm Hg. A total of 350 ml of physiological solution was administered. The pressure in the carotid artery rose to 60-58 mm Hg after 1 hr 40 min; 23) spinal cord completely removed. Artificial respiration applied. Arterial pressure dropped from 130-140 to 30-35 mm Hg. A total of 400 ml of physiological solution was injected into the external jugular vein. The pressure in the carotid artery rose to 70-75 mm Hg and uropoiesis was restored after 45 min; 24) upper mesenteric, pulsating; 25) spinal cord completely removed. Artificial respiration applied. Both vagal sympathetic trunks severed in cervical region. The pressure in the carotid artery dropped from 130-140 to 20-30 mm Hg. Uropoiesis ceased. A total of 400 ml of physiological solution was administered. Blood pressure rose to 70-75 mm and uropoiesis was restored after 50 min.

The experiments of this series confirmed that the stimulatory effect on uropoiesis of a rise in pressure in the sinistral gastroepiploic artery is weaker than that of an increase in pressure in the mesenteric arteries. A less pronounced effect was noted regardless of when the pressure in the sinistral gastroepiploic artery was raised (at the beginning or end of the experiment, or before or after the pressure in the isolated mesenteric arteries was increased). Stimulation of the receptors of the sinistral gastroepiploic artery can have either a weakly stimulatory or an inhibitory influence on uropoiesis. We thus detected a peculiarity in the physiological action of the receptors of this artery: when they are stimulated there is a marked reflex response in the spleen, its volume increasing. The reaction of the kidneys is less pronounced and may have an inhibitory character.

In the experiments of the third series, as in those of the second series, the absolute quantity of urine excreted decreased after transection or partial or complete destruction of the spinal cord. The increase in uropoiesis in response to a rise in pressure in the isolated arteries also decreased in comparison to that observed with the central nervous system intact. However, the relative increase in the amount of urine excreted when the pressure in the isolated arteries was raised did not decrease after the central nervous system was disengaged, but even increased at times in comparison with the amount excreted when the same stimuli were applied before destruction of the central nervous system.

There were cases in which the kidneys did not react to a rise in pressure in an isolated artery before destruction of the spinal cord, but responded to the same stimuli with a marked increase in uropoiesis after the cord was destroyed.

For example, in our experiment of 29 March 1950, before disengagement of the central nervous system a rise in pressure in the superior mesenteric artery was accompanied by excretion of one drop of urine from the left kidney every 5 min, while stimulation of the inferior mesenteric artery did not affect uropoiesis. After disengagement of the central nervous system, stimulation of the superior mesenteric artery was accompanied by excretion of five drops of urine from the left kidney over a 5-min period; stimulation of the inferior mesenteric artery caused secretion of one drop of urine every 5 min.

This effect became especially pronounced when the kidneys were preliminarily exposed to other stimuli, e.g., injection of physiological solution, hypertonic saline solution, urea, etc., into the blood stream.

In the overwhelming majority of cases, a constart rise in pressure in the isolated arteries was considerably more effective than a "pulsating" rise in pressure. The latter failed to affect renal activity more frequently than the former, in rare cases even inhibiting it. An increase in pressure in isolated arteries can have a stimulatory effect on the uropoietic function of the kidneys both before and after destruction of the central nervous system and when there are no changes whatsoever in the blood pressure in the general vascular system. This effect consequently cannot be due to primary changes in general circulation.

On the basis of the data presented in this chapter, we must conclude that stimulation and inhibition caused by changes in pressure in isolated abdominal arteries can be transmitted to the uropoietic apparatus by a peripheral neural mechanism. Since we employed only stimuli adequate for the vascular mechanoreceptors in our experiments, this mechanism cannot be the axon reflexes of efferent sympathetic fibers. The only possible mechanism involves the reflex arcs of peripheral, or local reflexes.

On the basis of the histological investigations of renal innervation conducted by V. Smirnov (1901) and the observations made by B.D. Kravchinskiy (1949) and L.A. Orbeli's colleagues, we can assume that the uropoiesis-stimulating effects we have described are due to reflexes affecting both the renal vascular system and the tissue of the renal tubules. It is obvious that this hypothesis requires further experimental verification.

Chapter 7

LYMPHOPOIETIC REFLEXES ORIGINATING IN THE VASCULAR RECEPTOR FIELDS OF THE ABDOMEN

Determination of the structural characteristics of the lymphatic system, the characteristics of lymphopoiesis and lymph circulation, the anatomic and functional relationships between the lymphatic and circulatory systems, etc., are all problems in which physiologists and pathologists are particularly interested. In recent years large-scale monographs have been published on the lymphatic system (D.A. Zhdanov, 1952; I. Rusn'yak, M. Fel'di, and D. Sabo, 1957).

The investigations described in this chapter were limited in scope. We will consider only the possibility of peripheral reflex transmission of excitation from the receptors of the abdominal blood vessels to the lymph stream, including in the latter both lymphopoiesis and the actual circulation of the lymph. The nervous system can exert a regulatory action on lymph secretion and circulation in various ways: by modifying metabolic activity in the appropriate tissues and organs, by altering the blood pressure, the osmotic pressure of the blood and tissues, or the permeability of the capillary walls, by modifying various types of movements, etc. None of these possible ways in which the nervous system can exert a regulatory influence has as yet been studied sufficiently well.

In Chapter X of their monograph, I. Rusn'yak, M. Fel'di, and D. Sabo (1957) utilized a thorough analysis of the literature and their own experimental research as a basis for concluding that one of the principal factors responsible for lymph flow is the different forms of active and passive movements involved in muscular contractions, including those of the heart and intestines, blood flow, breathing, etc., the direction of the lymph stream being governed by the valves of the lymph vessels.

Researchers had long ago established the existence of efferent innervation for the thoracic duct (Wrisberg, 1780; Cruikshank, 1789, 1790; cited by I. Rusn'yak, M. Fel'di, and D. Sabo) and other more or less large-diameter lymph vessels (D.A. Timofeyev, 1897; A. Dogel', 1897; V.N. Tonkov, 1898; et al.). It was found that the lymph vessels are innervated by the parasympathetic and sympathetic nervous systems. The plexi surrounding the large lymph vessels contain nerve cells (A.P. Lavrent'yev, 1925-1926, 1927, et al.).

Repeated attempts were made to determine the importance of this efferent innervation, employing transection of nerve trunks (V.V. Pashutin, 1872; et al.) and various types of stimulation (S.V. Levashev, 1886; et al.). The experiments conducted often yielded contradictory results, especially when the state of the lymph vessels after transection or during stimulation of nerve trunks was evaluated from the changes in lymph circulation. Direct observation of the state of the lymph vessels during stimulation of the nerves leading to them led Bert and Laffont (1882) to conclude that these vessels constrict when the mesenteric nerves are stimulated and dilate when the splanchnic nerves are stimulated (cited by I. Rusn'yak, M. Fel'di, and D. Sabo). Reporting on their own experiments, I. Rusn'yak, M. Fel'di, and D. Sabo (1949, 1950) stated that stimulation of the sinistral sympathetic trunk may cause contraction and spasm of the lymph vessels of the internal organs on the same side of the body (1957). The effect of various drugs has also been studied. Z.T. Valeyeva (1948, 1954) established that the thoracic duct dilates when perfused with caffeine or quinine and constricts when perfused with adrenilin, barium chloride, of physostigmine.

Little research has been done on reflex effects (particularly those associated with pain) on lymphopoiesis or on reflexes originating in the lymphatic system itself. Among the first observations in this area were those of Camus and Glev (1894), who established that the thoracic duct contracts when sensory nerves are stimulated. M.G. Durmishyan and Ya.A. Egolinskiy (1938a) observed retardation or complete cessation of uropoiesis and effusion of lymph from the thoracic duct on application of painful stimuli. This effect can be produced in manifest form only when the cerebral cortex remains functionally intact; it can be prevented by deep anesthesia. Retardation of lymphopoiesis is not associated with a change in muscular activity, particularly that of the respiratory muscles, since it can be induced in curarized animals. Humoral factors (the adrenal and hyphysial hormones) participate in the retardation of lymphopoiesis. M.G. Durmishyan and Ya.A. Egolinskiy (1938b) noted a decrease in lymph flow and a slight increase in uropoiesis in experimental animals after transection of the vagus nerves. In this case the chloride content of the blood and lymph decreased and, conversely, that of the urine increased.

Stimulation of the peripheral ends of the transected vagus nerves increased the outflow of lymph from the thoracic duct and reduced uropoiesis. A.M. Zimkina, A.A. Mikhel'son, and Ya.A. Egolinskiy (1938) observed that the greater the outflow of lymph, the less urine is secreted. Conditions favoring an intensification of uropoiesis reduce lymph flow, while conditions promoting an increase in lymph flow reduce uropoiesis.

In contrast to M.G. Durmishyan and Ya.A. Egolinskiy, M.I. Kokhanina (1941, 1948, 1949, 1951, et al.) observed a sharp increase in lymph flow in experimental animals on painful stimulation of the central end of the sciatic nerve. Stimulation of the peripheral end of the vagus nerve yielded a three-phase reaction consisting of brief attenuation, substantial intensification (by 50-200%), and gradual abatement of lymph flow. Stimulation of the central end of the vagus nerve caused lymph flow to increase by a factor of 2-3, but only while the stimulus was acting. After stimulation was discontinued, lymph flow decreased to below its initial level. Lymphopoiesis is intensified by electrical stimulation of the point where the common carotid artery and the sinus nerve diverge, this being accompanied by a sharp drop in blood pressure. On the basis of her experimental results, M.I. Kokhanina surmises that intensification of lymph flow is due to a reflex action on the contractile elements of the lymph vessels. Lymphopoiesis is reflexively intensified when the pressure in the splenic vessels is raised or when hypercapnic Tyrode's solution is passed through them. In 50% of all experiments lymphopoiesis was increased by a rise in pressure in the renal pelvis or in the vessels of an isolated intestinal loop. The acceleration of lymph flow on painful stimulation results from the increase in blood pressure and the changes in breathing. Stimulation of the intestinal mechanoreceptors of a puppy begins to induce reflex changes at two weeks of age (I.A. Beremzhanova, 1955).

A rather detailed survey of the literature on lymph circulation and its regulation is given in the monographs by A.P. Polosukhin and V.V. Petrovskiy. Briefly, it can be stated that changes in the condition of the lymph vessels (and hints in lymph flow) can be induced by stimulation of various regions of the vascular system, particularly the interoceptors of the pulmonary vessels (A.Ye. Beketayev, 1955; D.I. Smirnov, 1955), the superior vena cava (D.I. Smirnov, 1955; V.V. Petrovskiy, 1957), the sinocarotid zone (R.S. Vasil'chenko, 1955), the hepatic, renal, mesenteric, and femoral arteries and veins (G.N. Kotova, 1957), the intestinal interoceptors (I.A. Beremzhanova, 1955), a number of other internal organs (M.I. Kokhanina, 1955, 1956; L.E. Bulekbayeva, 1961), the pericardial interoceptors (R.S. Vasil'chenko and A.N. Dankova, 1955), the pleura and pericardium (L.P. Musatova, 1961), and the genitalia (N.A. Bublik, 1961).

It must be noted that clamping of the abdominal arteries (hepatic, renal, splenic, mesenteric, and femoral) causes constriction of the lymph vessels, while formation of embolisms in these arteries causes them to dilate. They also dilate when the pressure in the carotid artery and aorta is raised or when the hepatic, renal, splenic, mesenteric, and fenoral veins are clamped. On the other hand, clamping of the superior vena cava is accompanied by constriction of the lymph vessels (K.V. Kovanov, 1952; G.N. Kotova, 1955). Different areas of the vascular system thus have different reflex effects on the lymphatic system.

V.V. Petrovskiy (1954, 1957) and V.P. Glagolev (1958) concluded that the circulatory and lymphatic systems exert reciprocal reflex influences on one another, functioning as a unit and, through coordinated activity, facilitating maintenance of blood pressure at a definite physiological level. Hemodynamic disturbances result in changes in the tonus of both the blood and lymph vessels, those in the latter in turn leading to changes in vascular tonus.

These reflex interactions also occur when the pressure in the superior vena cava is varied.

The possibility of reflex reactions of this type has been confirmed by the histological investigations of V.M. Godinov (1950), who established that the lymph nodes contain receptors of two types: brush-like structures, which are probably baroreceptors, and receptors surrounded by round or oval cells of the glomic type, which are apparently chemoreceptors. The reflex reactions of the cardiovascular system to stimulation of the lymphatic system have been described by I.V. Sergeyeva and V.N. Chernigovskiy (1951), R.S. Vasil'chenko and A.N. Dankova (1955), V.P. Glagolev (1958), and R.S. Sabinina-Vasil'chenko (1961). V.P. Glagolev (1958) established that conditioned reflexes to lymphopoiesis can be developed.

In 1949, working in our laboratory, Yu.S. Uryupov studied the influence of changes in pressure in isolated arteries (the superior and inferior mesenteric and sinistral gastroepiploic arteries) on lymph flow. It was initially planned to observe the outflow of lymph from the liver and intestine separately, for which purpose cannulas were inserted into the appropriate lymph vessels. However, 10 experiments conducted in this manner failed to yield satisfactory results. The investigation was hampered by clotting of the lymph and by the fact that the lymph vessels often ruptured during the observation period. Moreover, the collection of lymph by this method was complicated by the fact that cannulas were also inserted into the abdominal blood vessels in order that the pressure in the isolated vessels could be varied. The manipulation of these vessels had an unfavorable effect on the lymph-collection process. Uryupov was consequently forced to collect lymph from the thoracic duct, using the technique described by Ya.A. Egolinskiy (1929).

In addition to studying the effect of changes in pressure in the isolated mesenteric and sinistral gastroepiploic arteries, Yu.S. Uryupov also observed lymph flow during and after clamping of the common carotid arteries. Table 7 presents the data obtained in these experiments.

A total of 16 experiments were carried out to study the effect of clamping of the common carotid arteries; in eight experiments the lymph

TABLE 7

Дата 1 проведения опыта	2 Продолжительность наблюдения (в минутах)	3 Количество капель лимфы, выделившееся за время наблюдения		
		4 до зажатия артерий	5 во время зажатия общих сонных артерий	после снятия зажима с сонных артерий 6
1/XI 1949 г.	30	42		
	30	56	64	70
	30	56	75	74
7 Перерезаны оба блуждающих нерва				
	30	37	36	
5/XI 1949 г.	30	123	163	191
	30	145	135	163
7 Перерезаны оба блуждающих нерва				
	30	165	186	—
15/XI 1949 г.	30	78	39	32
	30	57	23 (за 25 минут) 8	66
16/XI 1949 г.	30	35	57	30
	30	53	60	78
	30	42 (за 32 минуты)	57	35
25/XI 1949 г.	30	9 94	89	94
26/XI 1949 г.	35	140	116	225
	30	10,0	8,0	7,0
29/XI 1949 г.	30	11,0	10,0	4,0[1]
	30	13,0	14,0	13,0[1]

* The lymph produced in the experiments of 26 November and 29 November 1949 was measured in milliliters.

1) Date of experiment; 2) observation time (in min); 3) number of drops of lymph secreted during observation period; 4) before clamping of arteries; 5) during clamping of common carotid arteries; 6) after removal of clamps from carotid arteries; 7) both vagus nerves transected; 8) after 25 min; 9) after 32 min.

flow increased, in seven it decreased, and in one it remained almost unchanged. A total of 14 experiments were conducted after the clamps were removed from the common carotid arteries; in seven experiments the lymph flow increased, in six it decreased, and in one it remained almost unchanged. Consequently, application of identical stimuli to the carotid artery can cause qualitatively different changes in lymph flow, while application of qualitatively different stimuli can cause identical changes in lymph flow.

The effect of changes in pressure in the isolated superior and inferior mesenteric and sinistral gastroepiploic arteries was studied in large dogs weighing no less than 10-15 kg. Before the experiments began the animals were injected subcutaneously with a 2% morphine solution in a dose of 0.5 ml per kg of live weight. General anesthesia was induced with a mixture of three parts ether, two parts chloroform, and one part alcohol.

A tracheotomy was performed to expose the sinistral jugular vein. The cephalic end of this vein and the subclavian vein were tied off. A cannula, from which lymph from the thoracic duct was subsequently discharged, was inserted into the jugular vein. The amount of lymph discharged was calculated first by counting the number of drops and then by determining the volume in milliliters produced over a predetermined interval.

Isolation of the superior and inferior mesenteric and sinistral gastroepiploic arteries and the preparations for varying the pressure in these arteries were carried out before the observations began, as was described in prior chapters. Cannulas were inserted into the peripheral ends of the isolated arterial segments. Several additional arteries were sometimes isolated during the course of the experiments. Continuous records of respiration and of the pressure in one common

TABLE 8

Дата проведения опыта 1	2 Продолжительность наблюдения (в минутах)	3 Количество выделившейся лимфы (в мл)				
		4 до перевязки артерии	5 артерия перевязана	6 в артерии повышено давление		9 в артерии давление 0
				7 величина давления (в мм рт. ст.)	8 количество лимфы (в мл)	
2/XII 1949 г.	30	—	4,0	110	6,0	5,0
» »	30	—	7,0	120	6,5	4,5
17/I 1949 г.	30	—	57,0	95—100	32,5	—
18/I 1950 г.	60	—	28,5	100—110	20,0	—
24/I 1950 г.	30	20,0	9,0	110—120	17,0	4,0
» »	30	—	—	140—150	14,0	—
28/I 1950 г.	30	2,0	0,5	100—110	4,5	1,5
31/I 1950 г.	30	7,7	5,5	80—100	6,5	1,8
» »	30	—	2,1	100—120	3,8	1,3
16/II 1950 г.	30	8,5	5,5	95—100	10,25	6,8
4/III 1950 г.	30	22,0	18,0	100—110	28,0	18,0
28/V 1950 г.	30	36,0	30,0	80—110	38,0	24,0
10 Разрушен спинной мозг начиная со II—III грудного сегмента						
28/V 1950 г.	30	—	55,0	80—110	77,0	

1) Date of experiment; 2) observation time (in min); 3) amount of lymph secreted (in ml); 4) before ligation of artery; 5) artery ligated; 6) arterial pressure raised; 7) pressure (in mm Hg); 8) amount of lymph (in ml); 9) arterial pressure zero; 10) spinal cord destroyed from 2nd-3rd thoracic segment down.

carotid artery were made in some experiments.

Table 8 presents the results of nine experiments in which we observed the effect of variations in pressure in the isolated inferior mesenteric artery on lymph flow.

Table 8 contains data on the lymph flow before ligation of the inferior mesenteric artery, i.e., the initial "normal" lymph discharge with natural pressure in the inferior mesenteric artery, after ligation of this artery, and when the arterial pressure was raised and then reduced to zero. Disengagement of the artery was inevitably accompanied by a decrease in the amount of lymph produced. At first glance, it appears that this decrease in lymph flow can be attributed to the reduction of tissue blood supply resulting from ligation of the artery. However, this conclusion cannot be regarded as valid for the following reasons. First, as control observations showed, no decrease in lymph flow occurred if the artery was ligated nearer the periphery and a high pressure was maintained in its central segment. Secondly, a subsequent rise in pressure in the isolated arterial segment was in most cases accompanied by an increase in lymph flow, despite the fact that the blood supply from the artery to the tissues was not restored.

Table 8 shows the results of 13 such observations, in 11 of which raising the pressure in the isolated artery (within physiological limits) caused a clear increase in the amount of lymph secreted. The decrease in lymph flow resulting from ligation of the inferior mesenteric artery is consequently due to reflex signals from the arterial baroreceptors. As the data presented in Table 8 show, this conclusion was confirmed by subsequent observations. The pressure in the isolated artery was reduced to zero. In all nine experiments it was found that such reduction of the pressure in the inferior mesenteric artery caused the amount of lymph produced to decrease.

Raising the pressure in the isolated inferior mesenteric artery thus reflexively increased the lymph flow; only in rare instances (the experiments of 17 January and 18 January 1950) did the lymph flow decrease while the elevated pressure was acting. A reduction in pressure in the isolated inferior mesenteric artery was accompanied by a reflex decrease in lymph flow. Adequate stimulation of the baroreceptors of the inferior mesenteric artery can be effective whether or not general changes in pressure in the circulatory system are present.

An experiment conducted on 28 May 1950 showed that the reflex stimulatory effect of elevated pressure in the isolated inferior mesenteric artery may persist after destruction of the spinal cord from the 2nd-3rd thoracic segment down. This stimulatory effect may consequently

TABLE 9

Дата 1 проведения опыта	Продолжительность наблюдений (в минутах) 2	3 Количество выделившейся лимфы (в мл)				
		4 артерия не перевязана	6 5 артерия перевязана	6 в артерии повышено давление		9 в артерии давление 0
				величина давления 7 (в мм рт. ст.)	количество 8 лимфы (в мл)	
1/II 1950 г.	30	9,1	7,3	100—120	8,7	—
6/II 1950 г.	60	1,8	0,3	80—100	1,7	—
15/II 1950 г.	30	15,8	8,1	100—110	12,3	5,4
13/III 1950 г.	30	12,0	10,0	100	21,0	8,5
18/III 1950 г.	30	15,0	9,95	100—105	19,58	6,7
11/IV 1950 г.	30	12,5	8,0	80—100	15,3	—
5/V 1950 г.	30	9,2	4,6	80—110	9,3	6,6

1) Date of experiment; 2) observation time (in min); 3) amount of lymph secreted (in ml); 4) artery not ligated; 5) artery ligated; 6) pressure in artery raised; 7) pressure (in mm Hg); 8) amount of lymph (in ml); 9) arterial pressure zero.

be produced by both central and peripheral nervous mechanisms.

In order to get an idea of the sequence and other features of this group of observations, we present the following extract from the record of one experiment.

Record of experiment of 16 February 1950. Female dog weighing 12 kg. Animal injected subcutaneously with 6 ml of 2% morphine solution at 12:30. All preparations completed by 13:20. A total of 8.5 ml of lymph was secreted between 13:35 and 14:05. The pressure in the common carotid artery fluctuated between 70 and 74 mm Hg. Respiration rate reached 8-9 cycles per min.

The central end of the inferior mesenteric artery was ligated at 14:05. A total of 5.5 ml of lymph was secreted between 14:05 and 14:35. Ligation of the artery caused no change in respiration or in the pressure in the common carotid artery. The pressure in the isolated artery was raised to 100-110 mm Hg between 14:35 and 15:05. A total of 10.25 ml of lymph was secreted during this period. There were no changes in respiration or in the pressure in the common carotid artery. The pressure in the inferior mesenteric artery was reduced to zero at 15:35. A total of 6.8 ml of lymph was secreted over the period extending to 16:05. No changes in respiration or in the pressure in the common carotid artery were noted.

Table 9 is a summary of the results of observation of the changes in lymph flow produced by varying the pressure in the isolated superior mesenteric artery.

Comparison of the data in Tables 8 and 9 shows that the results obtained are identical. Lymph production was greater before the arteries were disengaged than afterward. When the pressure in the isolated arteries was raised (within physiological limits) there was a substantial intensification of lymphopoiesis, while reducing the arterial pressure to zero caused a decrease in lymphopoiesis. We can consequently conclude that, in general, stimulation of the baroreceptors of the superior and inferior mesenteric arteries can have a reflex effect on lymph secretion.

The following is an extract from the record of one experiment in this series.

Record of experiment of 18 March 1950. Female dog weighing 21 kg. Animal injected with 10 ml of 2% morphine solution at 8:00. All preparations completed by 11:30. The peripheral end of the superior mesenteric artery was ligated. A total of 15 ml of lymph was secreted between 11:30 and 12:00. The pressure in the common carotid artery was 112/84-114/100 mm Hg and the respiration rate was 17-19 breaths per min. The central end of the superior mesenteric artery was ligated at 12:10, thus isolating the artery. The pressure in the artery was held at zero from 12:10 to 12:40 and 9.95 ml of lymph was secreted. The pressure in the common carotid artery was 100/80 mm Hg immediately before isolation of the superior mesenteric artery and [illegible] mm Hg after this operation; the respiration rate was 21 breaths per min. Between 12:50 and 13:20 the pressure in the isolated artery was held at 100-105 mm Hg and 19.58 ml of lymph was secreted. The pressure in the common carotid artery was 78/66 mm Hg immediately before the pressure in the superior mesenteric artery was raised and 78/64 mm Hg while the elevated pressure was acting; the respiration rate was 24 and 23 breaths per min respectively.

Table 10 presents data obtained in studying the effect of changes in pressure in the sinistral gastroepiploic artery (3 experiments).

TABLE 10

Дата проведения опыта 1	Продолжительность наблюдения (в минутах) 2	Количество выделившейся лимфы в каплях 3			
		4 артерия выключена	5 в артерии повышено давление		8 давление в артерии 0
			6 величина давления (в мм рт. ст.)	количество капель 7 лимфы	
14/III 1949 г.	13	17	100	16	—
	5	—	160 9	5	3 10
15/III 1949 г.	10	47	160 (продолжительность наблюдения 20 минут)	1	(продолжительность наблюдения 25 минут)
18/IV 1949 г.	10	49	110	49	30 11 (продолжительность наблюдения 5 минут)

1) Date of experiment; 2) observation time (in min); 3) amount of lymph secreted, in drops; 4) artery disengaged; 5) arterial pressure raised; 6) pressure (in mm Hg); 7) amount of lymph, drops; 8) arterial pressure 0; 9) observation time 20 min; 10) observation time 25 min; 11) observation time 5 min.

Since the experimental results cited are so scanty, they can be used only for a rough evaluation of the effect of increased pressure in the isolated sinistral gastroepiploic artery on lymphopoiesis. First of all, these results are given consideration because they differ from those obtained when the pressure in the superior and inferior mesenteric arteries was varied. Secondly, they are similar to the data obtained in studying the influence of variations in pressure in the sinistral gastroepiploic artery on uropoiesis. As an approximation, we can thus assume that the reflex action of stimulation of the baroreceptors of the sinistral gastroepiploic artery on uropoiesis and lymphopoiesis is often either inhibitory or totally ineffective.

In conclusion, we must note the critical observations made by I. Rusn'yak, M. Fel'di, and D. Sabo (1957) regarding Yu.S. Uryupov's experiments: "... our criticism of Kokhanina's investigations, i.e., that her technique cannot be employed to resolve the question of whether the change in the amount of lymph discharged from the thoracic duct is due to alteration of lymphopoiesis or of lymph circulation (the tonus of the lymph vessels), is also valid to a greater or lesser extent for Uryupov's results." We have emphasized that Uryupov's investigations were in no way intended to resolve the question of the mechanism of changes in lymph flow (whether they result from changes in lymphopoiesis or in lymph circulation). Uryupov's research had a totally different purpose, i.e., to determine whether lymph flow changes when the pressure in isolated abdominal arteries is varied before and after destruction of the central nervous system. As the material presented above has shown, this was found to be the case. Reflex stimulation of lymph flow when the pressure in the isolated mesenteric arteries is raised may occur both before and after destruction of the spinal cord.

What is the mechanism of this intensification of lymph flow? Is it due to a change in lymphopoiesis or to a change in lymph circulation resulting from dilatation of the lymph vessels? Only an indirect answer to this question can be obtained from Yu.S. Uryupov's experiments, by comparing a number of data. Comparison of the time required for the effects observed to develop and of the characteristics of lymph flow and biligenesis, which we will consider in the following chapters, permits us to surmise that reflex stimulation originating in the baroreceptors of the mesenteric arteries may influence lymph production and circulation both before and after destruction of the spinal cord.

Yu.S. Uryupov employed a technique that suited the purpose of his investigations and which had been used to determine the physiological significance of the receptors of the carotid sinuses and other vessels. Application of this method corresponds to the physiological conditions of vital activity to a far greater extent than does indirect stimulation (electrical or otherwise) of nerve trunks and nerve centers.

On the basis of our observations, we reached the following conclusions:

1. Hemostasis in the carotid arteries causes lymph flow to vary, while hemostasis in the superior and inferior mesenteric arteries causes it to decrease.

2. A rise in pressure in the isolated mesenteric arteries causes an intensification of lymph flow. This effect can be detected without preliminary or parallel changes in respiration or in the pressure in the common carotid artery. It may also occur after destruction of the spinal cord.

3. The effect of disengagement or stimulation of the baroreceptors of the sinistral gastroepiploic artery on lymph flow is less definite. It may be slightly stimulatory or inhibitory and is often entirely absent.

4. It can be assumed that the nervous system regulates lymphopoiesis and lymph circulation both by varying the blood pressure at the sites of lymph production and by acting reflexively on the receptors of the vascular system.

Chapter 8

BILIGENETIC REFLEXES ORIGINATING IN THE ABDOMINAL VESSELS

In his lectures on the pathophysiology of digestion, I.P. Razenkov (1948) correctly pointed out that the organs and tissues of the digestive system do not function in isolation, but interact with one another under both physiological and pathological conditions. If a stimulus initially activates one of the organs of this system, this eventually leads to activation of the entire system. This conclusion was verified experimentally by I.P. Pavlov, I.P. Razenkov, and others.

The biligenetic and biliational functions of the liver are altered by stimulation of the gastric mucosa and by pathological conditions of the stomach (I.M. Lipets, 1939; I.T. Kurtsin, 1941; Ye.F. Larin, 1947; et al.), the distal end of the large intestine (R.S. Gartshteyn, 1949), and the ileocecal region (A.V. Rikkl', 1949, 1961; et al.). S.S. Poltyrev's colleagues (S.A. Frolov, 1948; Ye.S. Myasoyedov, 1948; A.A. Dudorova, 1948; V.N. Nikol'skiy, 1948; S.A. Konokotina and I.N. Pokrovskaya, 1949; N.A. Myasoyedova, 1947; N.A. Koroleva, T.A. Salova, and I.P. Gavrilyuk, 1949; R.S. Gartshteyn, 1949, 1956; et al.) described various interactions between the rectum, stomach, peritoneum, pleura, kidneys, salivary glands, and liver.

The biligenetic function of the liver is altered by artificial pneumothorax (S.I. Ochan, 1958). The gall bladder may exert a reflex influence on the hepatic biligenetic function (A.V. Gubar', 1956). Reflex changes in cardiac activity occur when the liver is perfused with solutions of histidine and histamine; when the gall bladder is inflated with a rubber bulb breathing becomes deeper and slower, cardiac activity is attenuated, blood pressure (particularly systolic pressure) drops, and the tonus of Oddi's sphincter often increases. The interoceptors of the liver and gall bladder act primarily on the parasympathetic nervous system (Yu.A. Petrovskiy and Ya.B. Maksimovich, 1954; Yu.A. Petrovskiy, Ya.B.Maksimovich, and Ye.N. Serdyuk, 1954). In M.B. Tetyayeva's opinion (1949), the functional characteristics of the digestive apparatus of higher animals can be evaluated from the development of the different stages of innervational relationships. Restoration of older, simpler functional relationships can be observed in these animals after more recent central structures are disengaged.

TABLE 11

Дата 1 проведения опыта	2 Продолжительность наблюдения в минутах	3 Название артерии	Количество выделившейся 4 желчи (в мл)				
			5 артерия не выключена	6 артерия выключена	7 в артерии повышение давления		10 в артерии давление 0
					8 величина давления (в мм рт. ст.)	9 количество желчи	
28/I 1950 г.	30	11 Нижняя брыжеечная	1,9	1,9	110—100	1,9	2,5
31/I 1950 г.	30	То же 12	1,7	2,8	80—100	2,5	3,1
16/II 1950 г.	30	» »	0,5	0,4	100—110	0,25	0,8 14
4/III 1950 г.	30	» » 13	2,1	1,1	100–110	0,7	2,5 (25 минут)
6/II 1950 г.	30	Верхняя брыжеечная	3,8	3,3	100—110	1,4	—
15/II 1950 г.	30	То же	2,8	2,0	110	2,3	0,7
13/III 1950 г.	30	» »	1,6	2,6	100	1,0	1,0
11/IV 1950 г.	30	» »	0	1,6	80—100	1,3	—

1) Date of experiment; 2) observation time, in min; 3) artery; 4) amount of bile secreted (in ml); 5) artery not disengaged; 6) artery disengaged; 7) arterial pressure raised; 8) pressure (in mm Hg); 9) amount of bile; 10) arterial pressure 0; 11) inferior mesenteric; 12) the same; 13) superior mesenteric; 14) min.

The experimental data cited thus indicate the complexity of the interaction of the organs of the digestive system and the interaction of this system with other functional systems. Yu.S. Uryupov and M.A. Vayn-Rib, working in our laboratory, made an experimental study of the reflex influence of stimulation of the superior and inferior mesenteric arteries on biligenesis. The fact that identical experiments were conducted separately by two individuals provided a good check on the results obtained.

The experimental procedure was the same as that described in prior chapters. The cannula through which the bile was obtained was generally inserted into the common bile duct. The differences in methodology will be pointed out when we discuss the results obtained. More than 20 experiments were conducted.

Table 11 shows the results of eight experiments. The results of a number of other observations will be presented later in graphic form.

The data in Table 11 show that ligation of the inferior mesenteric artery did not produce conclusive results: in one case biligenesis increased, in two cases it decreased, and in one case it remained unchanged. Bile secretion decreased in all four instances in which the pressure in this artery was raised; conversely, a decrease in pressure intensified biligenesis.

These observations may create the impression that a rise in pressure in the inferior mesenteric artery has an exclusively inhibitory effect on biligenesis. However, this conclusion would be incorrect. An increase in pressure in the inferior mesenteric artery may stimulate bile secretion. For example, this occurred in an experiment conducted on 22 September 1949, where 12 drops of bile were produced over a 25-min period after ligation of the inferior mesenteric artery and 11 drops were secreted over a 14-min period after the pressure in this artery was raised to 110 mm Hg; a total of four drops was produced over a 14-min period after the pressure in the isolated artery was reduced to zero. A similar reaction was observed in an experiment conducted on 11 October 1949, where 19 drops of bile were produced over a 10-min period after the inferior mesenteric artery was isolated from the vascular system; a total of 23 drops was secreted over a 10-min period after the pressure in the isolated artery was raised and 16 drops were produced over an equivalent period when the pressure was reduced to zero.

Our observations thus show that a rise in pressure in the isolated inferior mesenteric artery has a varying effect on biligenesis, depending on the conditions for vital activity and the experimental conditions, factors that we will consider later. A decrease in biligenesis under the influence of a rise in pressure in the inferior mesenteric artery is less common than an increase.

Approximately the same results were obtained in observations of the effect of variations in pressure in the superior mesenteric artery. As the data presented in Table 11 show, isolation of this artery from the common circulatory system led to a decrease in bile secretion; in two other experiments it caused an intensification of biligenesis. Raising the pressure in this artery to 100 mm Hg caused a decrease in bile secretion in three cases and an increase in only one case.

For purposes of illustration, the results obtained are shown in Figs. 20-24.

The curves in Fig. 20 show that no bile was secreted before the pressure in the isolated superior mesenteric artery was raised. A pulsating increase in pressure (100-80 mm) in this artery was accompanied by production of two drops of bile. An additional two drops of bile were secreted when the pressure in the artery was reduced to 80 mm Hg,

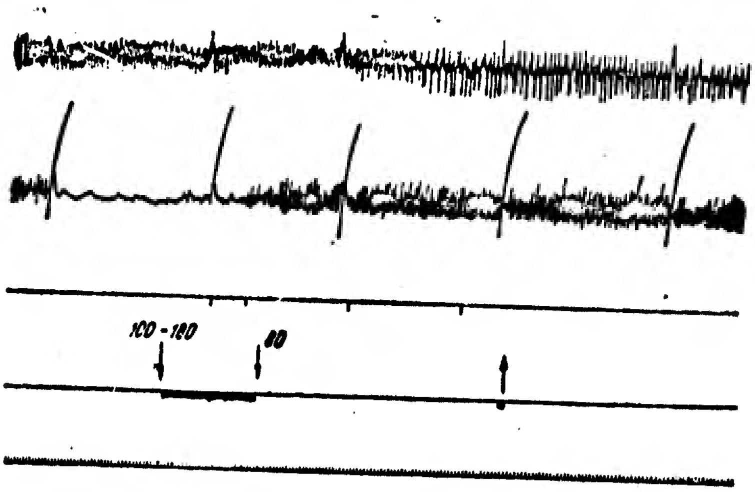


Fig. 20. The top curve represents the pressure in the common carotid artery, the second curve is a pneumogram, the third curve indicates the number of drops of bile secreted, the fourth curve indicates application of the stimulus, and the bottom curve is a one-second time marker.

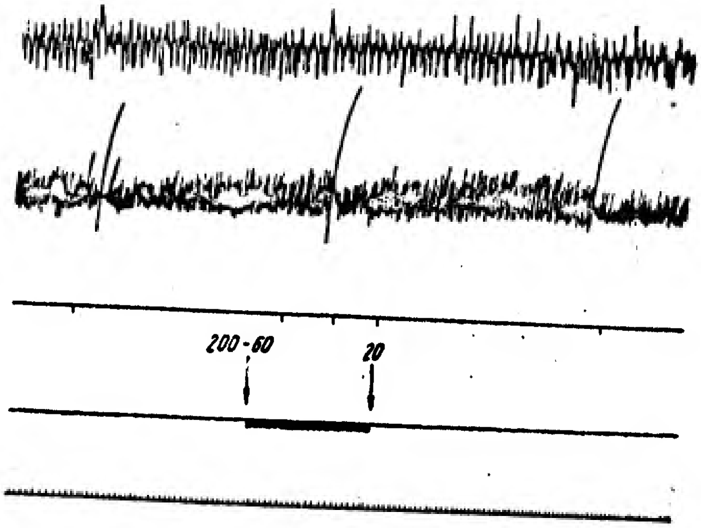


Fig. 21. Curves the same as in Fig. 20. The arrows indicate the beginning and end of a pulsating rise in pressure (200-60 mm Hg).

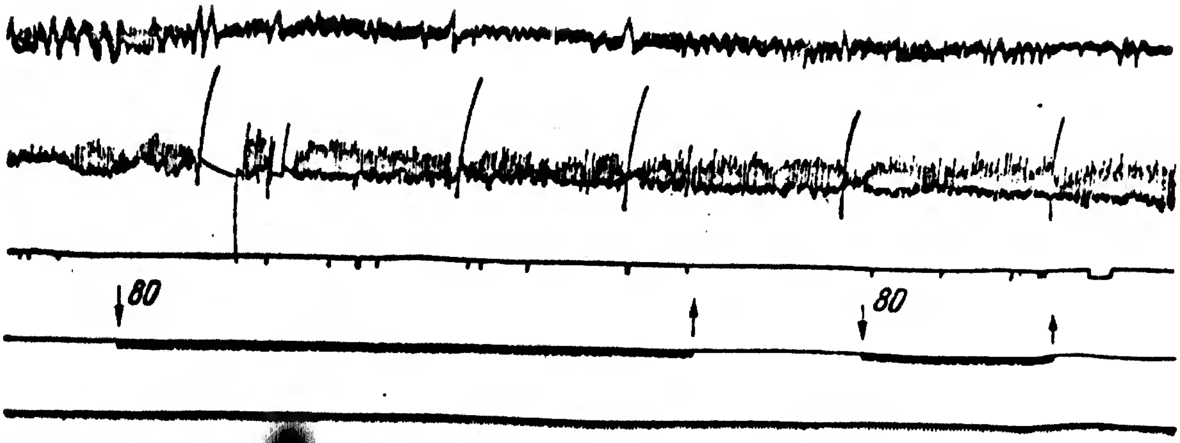


Fig. 22. Curves the same as in Fig. 20. The numeral 80 is the blood pressure in mm Hg.

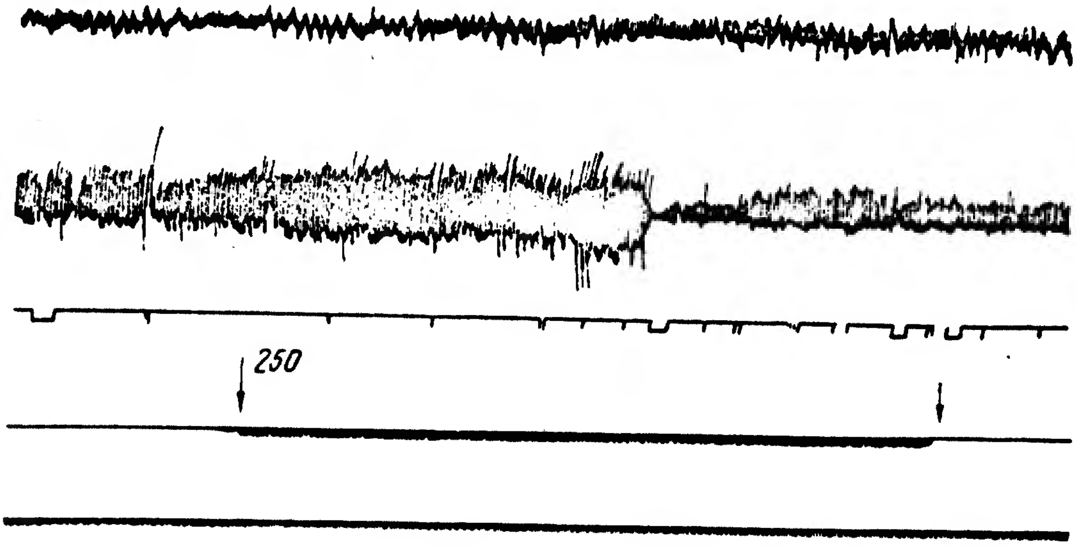


Fig. 23. Curves the same as in Fig. 20. The numerals 0-250 indicate the blood pressure in mm Hg. The arrows indicate application and discontinuation of pressure.

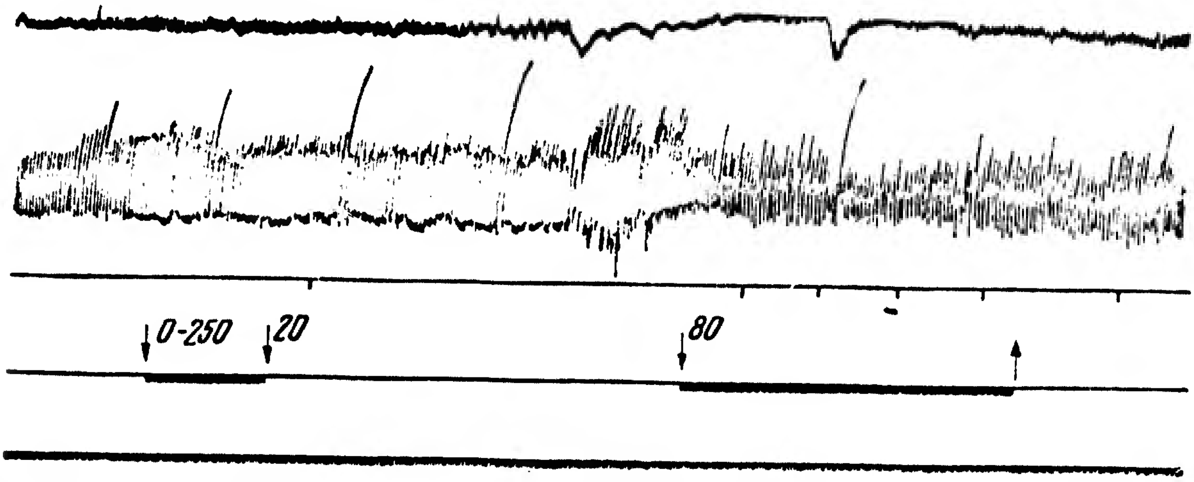


Fig. 24. Curves the same as in Fig. 20. The arrows indicate application and discontinuation of pressure. The numerals indicate the blood pressure in mm Hg.

but there was a considerable interval between one drop and the other. When the pressure in the isolated artery was reduced to zero biligenesis ceased (indicated by the arrow pointing upward).

No fluctuations in general arterial pressure that could be attributed to the rise in pressure in the isolated artery were noted during our observations. The greatest respiratory-movement amplitude (at the beginning of the graph) was due to technical deficiencies.

Figure 21 shows that a pulsating (200-60 mm Hg) increase in pressure in the isolated superior mesenteric artery stimulated biligenesis without any prior or concomitant changes in respiration or in the pressure in the common carotid artery. Three drops of bile were secreted in response to the rise in pressure. The changes in respiration and blood pressure occurred about half-way through the stimulation period and can be assumed to have been fortuitous. Similar changes were observed before the stimulus was applied. These changes occurred when the biligenetic reaction to the stimulus had already begun. An additional drop of bile was produced after the pressure in the isolated artery was reduced to 20 mm Hg.

The curves in Fig. 22 show the stimulatory effect of a rise in pressure in the isolated superior mesenteric artery on biligenesis. Thus, raising the pressure to 80 mm Hg caused an intensification of bile secretion; the latter was not, however, associated with changes in respiration or in the pressure in the common carotid artery. Reduction of the pressure in the isolated artery was accompanied by cessation of bile secretion, with no changes in respiration or in the pressure in the common circulatory system.

Figure 23 illustrates the effect of a sharp (to 250 mm Hg) increase in pressure in the isolated superior mesenteric artery. There were no noticeable changes in the pressure in the common carotid artery during the stimulation period, a slight rise in pressure being observed after approximately 3-1/2 min. An increase in depth of breathing occurred somewhat before the stimulus was applied. This intensified respiration continued for more than 4 min, extending into the stimulation period, and the depth of breathing then decreased considerably. A total of three drops of bile were secreted over a 2-1/2-min period before the stimulus was applied. Stimulation initially had an inhibitory effect. The first drop of bile was secreted approximately one minute after stimulation began. Bile was then discharged at a more rapid rate than before stimulation. Substantially intensified biligenesis continued for 5 min after the stimulus was discontinued. The latter phenomenon, clearly manifested in the experiment in question, indicates that strong adequate stimulation of the receptors of the vascular field is accompanied by a prolonged after-effect. When the curves representing respiration, blood pressure in the common carotid artery, and biligenesis are compared (Fig. 23), it can be seen that the changes in biligenesis were not parallel to those in respiration or carotid pressure.

It was necessary to determine whether the change in biligenesis produced by stimulation of the baroreceptors of isolated arteries results from a reflex influence on the liver, on the gall bladder, or on both simultaneously.

In order to resolve this question we conducted experiments in which the ductus cisticus and ductus hepaticus were ligated separately before their juncture with the common bile duct. Figure 24, which illustrates an experiment conducted on 12 June 1949, gives some idea of the results obtained.

In our experiment of 12 June 1949 the pressure in the isolated superior mesenteric artery was raised to 80-100 mm Hg after ligation of the cystic duct. No bile was secreted either before or during stimulation. The arterial pressure was then raised to 250 mm Hg. The curves in Fig. 24 show the effect of this stimulus. There were no changes in respiration or in the pressure in the common carotid artery and no bile was secreted during the stimulation period; when the pressure in the isolated artery was reduced to 20 mm Hg one drop of bile was secreted. It can be assumed that this strong stimulus was not without effect. This is indicated by the subsequent course of the experiment. Increasing the pressure in the isolated artery to 80 mm Hg caused secretion of four drops of bile, one drop being secreted after the stimulus was discontinued. Somewhat before this stimulus was applied there was an acceleration and attenuation of respiratory movements and an increase in pressure in the common carotid artery. These changes became more pronounced during the stimulation period.

In other experiments we investigated bile secretion when the pressure in the isolated superior mesenteric artery was raised after ligation of the hepatic duct above its union with the cystic duct. These observations also showed biligenesis to be possible.

This series of experiments thus demonstrated that changes in pressure in the isolated superior mesenteric artery can stimulate or inhibit biligenesis both as a result of their direct reflex action on the hepatic hepatic biligenetic function and as a result of their influence on the contractile activity of the gall bladder. At the same time, there are sometimes changes in respiration and in the pressure in the common vascular system, but these may be absent.

The character of the effect produced by stimulation sometimes varies within a single experiment. For example, 19 drops of bile were secreted over a 10-min period at the beginning of our experiment of 11 October 1949. When the pressure in the superior mesenteric artery was raised to 100 mm Hg 23 drops of bile were secreted over 10 min. When the arterial pressure was reduced to zero 16 drops were secreted over 10 min. When the pressure was again raised to 120 mm Hg 22 drops were produced over 10 min. When the pressure was increased to 200 mm Hg 21 drops were secreted over the same period, while when it was again reduced to zero 20 drops were produced. Elevated pressure in the superior mesenteric artery thus had a clearly stimulatory effect on biligenesis only at the very beginning of the experiment.

Yu.S. Uryupov's investigations showed that bile secretion may also be altered when the pressure in other blood vessels is varied.

The following are a few examples of this phenomenon.

In an experiment conducted on 21 January 1950 9 ml of bile was secreted over a one-hour period before the common carotid arteries were clamped; 8 ml was produced when the arteries were clamped for one hour; 9.7 ml was secreted over a one-hour period after the clamps were removed from the arteries.

In an experiment conducted on 19 April 1949 12 drops of bile were secreted over a 5-min period before the pressure in the isolated splenic artery was raised. A total of 19 drops was produced over 10 min with the pressure in this artery at 120 mm Hg. The rise in pressure in the splenic artery in this experiment thus somewhat inhibited biligenesis.

On the other hand, in an experiment conducted on 28 June 1949 raising the pressure in the splenic artery to 120 mm Hg somewhat intensified biligenesis.

Results of this type are easily recorded. Elevated pressure in isolated abdominal arteries may continue to affect biligenesis after destruction of the spinal cord. We will give special consideration to this phenomenon in subsequent chapters.

We can thus draw the following conclusions:

1. Biligenesis can be altered by varying the pressure in the iso-

lated superior and inferior mesenteric arteries.

2. A rise in pressure in the isolated arteries may cause both stimulation and inhibition of bile secretion in the same experiment.

3. This effect may occur with or without concomitant changes in respiration and in the pressure in the common carotid artery and before or after isolation of the central nervous system from the abdominal organs.

4. The latent period of the reaction produced ranges from several seconds to a minute or more. Prolonged after-effects may be observed.

Chapter 9

RESULTS OF PARALLEL OBSERVATIONS OF BILIGENESIS AND LYMPHOPOIESIS DURING CHANGES IN PRESSURE IN THE ABDOMINAL ARTERIES AND ORGANS

The need for parallel observations of the action of elevated pressure in isolated abdominal organs and arteries on biligenesis and lymphopoiesis arise primarily from the fact that adequate stimulation of isolated arteries may have both stimulatory and inhibitory effects on these secretory functions. It was necessary to determine whether the variations in the reflex responses of the liver and the lymphatic system were interdependent.

In experiments conducted on 28 January, 31 January, 16 February, and 4 March 1950 we made parallel observations of this type in studying the effect of variations in pressure in the isolated inferior mesenteric artery. A rise in arterial pressure was accompanied by a decrease in biligenesis and a substantial increase in lymphopoiesis.

In experiments conducted on 6 February, 15 February, 13 March, and 11 April 1950 we made similar observations on the effect of variations in pressure in the isolated superior mesenteric artery. We found that a rise in arterial pressure caused a substantial intensification of lymph flow. The quantity of bile secreted decreased in three experiments and increased slightly only in the experiment of 15 February 1950. These observations showed that stimulation of the same baroreceptors may cause identical or different reactions in lymphopoiesis and biligenesis.

Yu.S. Uryupov made similar observations on the effect of changes in pressure in the ureter, renal pelvis, and urinary bladder. Table 12 shows the results of stimulation of the interoceptors of the ureter and renal pelvis, while Table 13 shows the results of stimulation of the interoceptors of the bladder. Cannulas were inserted into the ureter and urinary bladder and connected to vessels filled with physiological solution.

The data in Table 12 show that, in the majority of cases, an increase in pressure in the ureters before transection of the spinal cord was accompanied by different biligenetic and lymphopoietic reactions.

In the experiments of 26 June, 11 July, 19 April, and 24 July 1951 an increase in pressure in the ureter was accompanied by a decrease in the amount of bile secreted, while lymph flow increased or remained unchanged (experiment of 26 January). Conversely, in other experiments (25 July, 28 July, and 30 July 1951) a rise in pressure in the ureter caused an increase in biligenesis and a decrease in lymphopoiesis, except for the experiment of 30 July, in which lymph flow also increased. In an experiment conducted on 3 May a rise in pressure in the ureter did not affect the amount of bile secreted, but somewhat increased lymph flow.

Varying reactions were also obtained in the majority of experiments in which the pressure in the ureters was reduced to zero. In the experiments of 25 July, 28 July, and 30 July 1951 a decrease in pressure was accompanied by a reduction in the amount of bile secreted and an increase in lymph flow. Conversely, in the experiments of 19 April and 26 June 1951 a decrease in pressure in the ureters caused biligenesis to increase and lymphopoiesis to decrease. The reactions in the experiments of 3 May and 24 July were monotypic, both biligenesis and lymphopoiesis decreasing in response to a drop in pressure in the ure-

TABLE 12

1 Дата проведения опыта	2 Продолжительность наблюдения (в мин.)	3 Количество (в мл)		6 Реакция на повышение давления				8 Давление снижено до 0		
		4 желчи	5 лимфы	7 величина давления (в мм рт. ст)	продолжительность наблюдения (в мин.)	количество (в мл) желчи	количество (в мл) лимфы	продолжительность наблюдения (в мин.)	количество (в мл) желчи	количество (в мл) лимфы
3/V 1951 г.	20	1,3	2,1	160	20	1,3	2,3	20	0,7	2,0
9 Произведена перерезка спинного мозга между III и IV грудными позвонками; перерезаны на шее блуждающие нервы										
	20	1,9	3,3	160—180	20	1,3	2,2	20	1,6	2,5
26/VI 1951 г.	20	0,6	11,0	10 Зажаты мочеточники	20	0,4	11,0	Зажимы сняты 11 20	0,6	6,0
19/IV 1951 г.	30	2,3	4,7	180	30	0,9	10,5	30	1,3	9,1
12 Спинной мозг перерезан между III и IV грудными позвонками и удален ниже места перерезки										
	30	1,6	6,7	180	30	1,3	4,0	30	2,7	5,9
11/VII 1951 г.	20	0,2	17,0	200	20	0	20,0	20	0	20,0
24/VII 1951 г.	30	0,8	5,0	210	20	4,0	7,0	30	1,0	4,0
25 VII 1951 г.	30	1,5	19,0	110—115	30	15,0	14,0	30	4,0	19,0
13 На шее перерезаны блуждающие нервы, спинной мозг между III и IV грудными позвонками										
28/VII 1951 г.	30	1,3	9,0	110—115	30	1,0	9,0	30	3,3	8,0
	20	1,5	16,0	120	20	1,6	13,0	20	1,3	14,0
13 На шее перерезаны блуждающие нервы, спинной мозг между III и IV грудными позвонками										
30/VII 1951 г.	20	2,0	11,0	120	20	1,7	8,0	20	2,5	12,0
	20	0,3	9,8	125	20	1,5	11,4	20	0,4	14,0

1) Date of experiment; 2) observation time (in min); 3) quantity (in ml); 4) bile; 5) lymph; 6) reaction to elevated pressure: 7) pressure (in mm Hg); 8) pressure reduced to 0; 9) spinal cord transected between 3rd and 4th thoracic vertebrae, vagus nerves transected in cervical region; 10) ureter clamped; 11) clamps removed; 12) spinal cord transected between 3rd and 4th thoracic vertebrae and removed below site of transection; 13) vagus nerves transected in cervical region, spinal cord transected between 3rd and 4th thoracic vertebrae.

ter; in the experiment of 11 July 1951 a drop in pressure affected neither biligenesis nor lymphopoiesis.

In three experiments we studied the biligenetic and lymphopoietic reactions after transection of the spinal cord between the 3rd and 4th thoracic vertebrae and of the vagus nerves of the cervical region. In another experiment the spinal cord was completely removed below the 3rd thoracic vertebra. After these operations the biligenetic and lymphopoietic reactions changed in the same direction in two experiments (increasing in the experiment of 3 May 1951 and decreasing in that of 25 July 1951) and in opposite directions in two experiments. The character of the reactions to elevated and reduced pressure in the ureters also varied: in the experiments of 3 May, 28 July, and 19 April biligenesis and lymphopoiesis decreased when the pressure in the ureters was raised and increased when this pressure was reduced; in the experiment of 25 July biligenesis increased and lymphopoiesis remained unchanged when the pressure in the ureters was raised and both secretory processes were somewhat intensified when this pressure was reduced.

This series of experiments thus showed that reflex interaction between the internal organs can still occur after the pathways joining them to the central nervous system have been destroyed or when the spinal cord is in a state of shock. It was also found that these interactions are somewhat altered under new conditions.

Before anatomic or functional isolation of the central nervous system the reactions of the internal organs to changes in pressure in the ureters follow the predominant pattern "excitation of one function and inhibition of the other." Reactions that follow a pattern of "simultaneous functional excitation or inhibition" begin to predominate after anatomic or functional isolation of the central nervous system. Reflex regulation is thus less advanced from the physiological stand-

TABLE 13

1 Дата проведения опыта	2 Продолжительность наблюдения (в мин.)	3 Количество (в мл)		6 Реакция на повышение давления				8 Давление снижено до 0		
		4 желчи	5 лимфы	7 величина давления (в мм рт. ст.)	продолжительность наблюдений (в мин.)	количество (в мл) желчи	количество (в мл) лимфы	продолжительность наблюдения (в мин.)	количество (в мл) желчи	количество (в мл) лимфы
3/V 1951 г.	30	1,0	3,7	180	30	1,5	2,8	30	1,5	1,6
10/V 1951 г.	15	1,7	2,9	180	15	1,5	5,0	15	2,3	3,4
9 Спинной мозг перерезан между III и IV грудными позвонками										
11/V 1951 г.	15	1,7	3,4	180	15	1,3	3,0	15	1,0	2,4
	15	0,9	4,8	180	15	0,6	5,8	15	1,1	3,3

1) Date of experiment; 2) observation time (in min); 3) amount (in ml); 4) bile; 5) lymph; 6) reaction to elevated pressure; 7) pressure (in mm Hg); 8) pressure reduced to 0; 9) spinal cord transected between 3rd and 4th thoracic vertebrae.

point.

Similar results were obtained in a few observations in which we studied the changes in biligenesis and lymphopoiesis during variations in pressure in the urinary bladder (Table 13).

In the experiment of 3 May 1951 a rise in pressure in the bladder was accompanied by an increase in biligenesis and a decrease in lymphopoiesis; conversely, in the experiments of 10 May and 11 May 1951 a rise in pressure in the bladder caused an increase in lymphopoiesis and a decrease in biligenesis.

When the bladder pressure was reduced to zero lymphopoiesis and biligenesis changed in opposite directions or biligenesis remained unaltered (experiment of 3 May).

The biligenetic and lymphopoietic reactions to variations in pressure in the urinary bladder were qualitatively altered after transection of the spinal cord (experiment of 10 May).

An increase in pressure in the urinary bladder caused an intensification of biligenesis and an attenuation of lymphopoiesis, which continued for 15 min after the bladder pressure was reduced to zero. A substantial after-effect was observed.

On the basis of this latter group of observations we can conclude that the biligenetic and lymphopoietic reactions to stimulation of the baroreceptors of the internal organs are interrelated. When the internal organs remain anatomically and functionally linked to the central nervous system, the biligenetic and lymphopoietic reactions to variations in pressure in an isolated organ or artery follow the preferential pattern "excitation of one function and inhibition of the other," i.e., obey the principle of reciprocity. After destruction of the anatomic or functional connections between the internal organs and the central nervous system, these reactions begin to follow the preferential pattern "simultaneous inhibition or excitation of both functions." In this case stimulation produces a pronounced after-effect, which can be regarded as a manifestation of the inertia of neural processes.

Chapter 10

BRIEF SUMMARY AND PROSPECTS FOR FURTHER RESOLUTION OF THE PROBLEM OF PERIPHERAL REFLEXES

In the introduction we posed the question of whether the peripheral ganglia of vertebrates, including mammals, are capable of reflex activity or merely conduct excitation in the efferent direction. This question was the guide for all the research conducted in our laboratory and described in this book. Our experimental investigations yielded a positive answer, i.e., the peripheral ganglia of mammals do have a reflex function.

A large amount of data has now been amassed on the diverse manifestations of interoceptive reflexes. Natural or artificial stimulation of internal organs can affect any portion of the central nervous system, including the cerebral cortex, in different ways and can thus be reflected in the activity of any functional system. There is no doubt that the central nervous system exerts a reflex regulatory control over the activity of the internal organs. A specific manifestation of this control is the excitation and inhibition of the internal organs by the central nervous system. Such regulatory activity can occur only if there is a two-way neural linkage between the organs and the central nervous system, which is essentially constructed on the "cyclic reflex" principle and in which "feedback pathways" are undoubtedly of special importance.

However, the regulation of the vital activity of the internal organs by the central nervous system does not preclude the existence of local neuroregulatory mechanisms whose activity is based on the reflex principle. This is specifically demonstrated by the recent histological investigations described in N.G. Kolosov's article entitled "Morphology of interneuronal connections" (1961). In comparing our experimental method with the techniques employed by other authors, we should emphasize that in the overwhelming majority of our experiments we used stimuli adequate to the baroreceptors, i.e., variations in blood pressure. In most investigations of peripheral neuroregulatory mechanisms sufficient consideration was not given to the character of the stimulus, so that the results of such observations could scarcely have been correctly interpreted.

In Chapter 3 we cited data indicating that the functional interaction of the pelvic organs persist after they are isolated. When the intermediate cellular tissue is left intact a change in pressure in one isolated organ can inhibit, intensify, or make manifest (if it was not noticeable before stimulation) the activity of other organs. A similar reaction was observed in isolated segments of the alimentary tract placed in a steam bath, i.e., under conditions that completely excluded the possibility of mechanical or humoral interactions between the isolated organs. The character of the reactions produced when one organ interacts with another is not uniform, but varies in accordance with the functional state of the effector, the strength of the stimulus, the transmission conditions in the synapses of the peripheral ganglia, etc. Preliminary administration of strychnine, especially intravenously, intensifies the reaction and increases the frequency with which it is observed after complete destruction of the central nervous system.

In the following chapters we presented experimental data obtained in our laboratory in studying the functional state of the urinary bladder, spleen, kidneys, liver (biligenesis), and lymphatic system under the action of variations in pressure in isolated abdominal vessels (the inferior and superior mesenteric arteries and veins, the sinistral gastroepiploic artery and vein, etc.) and in the ureters and urinary bladder.

The basic premise of these investigations was that the peripheral ganglia and plexi lying in direct proximity to a large blood vessel whose walls are rich in receptors supply it with fibers and also extend other fibers to various organs located at considerable distances. The relationships between the inferior mesenteric ganglion, the mesenteric artery, and the pelvic organs and between the ganglia, plexi, blood vessels, and organs in the upper portion of the abdomen are of this type. These anatomic data lead to the supposition that there may be functional neural links of the peripheral-, or local-reflex type between the blood vessels and organs of the abdomen. This hypothesis is supported by the histological investigations of A.S. Dogel', I.F. Ivanov, N.G. Kolosov, and their colleagues and agrees with the results of the physiological investigations of I.M. Sokovnin, N.A. Mislavskiy, I.P. Razenkov, Ye.I. Sinel'nikov, and others.

In studying the reactions of internal organs to changes in pressure in isolated abdominal vessels and organs, we also observed changes in the pressure in the common carotid artery and in respiration. Observations of this type only confirmed the data presented by many researchers to show that adequate mechanical or chemical stimulation of the abdominal interoceptors can produce reflex reactions effected by the central nervous system.

It has been conclusively established that reflexes arising in the vascular system serve primarily to regulate cardiovascular and respiratory activity. No matter in which portion of the vascular system the impulses develop, they are first transmitted to the vasomotor and respiratory centers. These reflexes are customarily referred to as "true cardiovascular reflexes." Under certain experimental conditions (e.g., intensification of the stimulus) reflexes originating in the receptors of the vascular system can be transmitted to other systems (muscular, etc.). V.N. Chernigovskiy suggested that reflex reactions of this type be called "conjugate reflexes."

On this basis, reactions developing in the respiratory and vascular systems in response to stimulation of the internal organs, particularly adequate stimulation of arteries and veins, are erroneously regarded as being exclusively pain reactions. They are pain reactions only if exceptionally strong stimuli are applied or if pain endings and fibers are specifically stimulated.

When a given stimulus was applied to the baroreceptors of the vascular system there were no changes in respiration or arterial pressure, but it would be incorrect to assume that these reactions were absent because the stimulus was not painful in nature. We are thus emphasizing the following fact: if excitation arising in the receptors of the vascular system is transmitted to the central nervous system, it must first induce blood-pressure and respiratory reactions (a true reflex). However, in our experiments we observed reactions other than those effected through the central nervous system; these particularly interested us.

S.S. Poltyrev (1948) also found that moderate stimulation of the distal end of the large intestine can induce secretory and motor activity in the stomach and intestinal glands and intensify biligenesis without any concomitant changes in general blood pressure. He attributed this to the fact that the stimuli employed were not painful.

However, there is also another explanation for this phenomenon. It is possible that the absence of changes in blood pressure resulted from the fact that excitation was not transmitted from the receptor apparatus of the stimulated regions to the central nervous system, but propagated through the digestive system from its point of origin along the local, or peripheral reflex apparatus. A number of the reactions of the alimentary apparatus described by N.A. Myasoyedova (1958) have such a mechanism. It is also possible that some of the motor and secretory reactions of the intestine described by O.B. Dobromyslova (1955) are attributable to this mechanism. The baroreceptive capacity of the small intestine ensures coordinated activity of all its segments. The character of the coordination of complex reflex responses extending from certain segments of the intestine to others is qualitatively variable. We cannot exclude the possibility that, under normal conditions, both central mechanisms and local, or peripheral reflexes participate in ensuring coordinated activity of all segments of the alimentary apparatus.

When the pressure in the isolated inferior and superior mesenteric, sinistral gastroepiploic, and other arteries, the urinary bladder, and the ureters is varied, the activity of the bladder, spleen, kidneys, and liver and lymphopoiesis may be altered without parallel or prior changes in respiration or in the blood pressure in the common carotid artery. For example, increasing the pressure in these arteries (within physiological limits) causes an increase in splenic volume, while a decrease in pressure causes a reduction of splenic volume.

A rise in pressure in the isolated inferior and superior mesenteric and sinistral gastroepiploic arteries causes an intensification of uropoiesis; a decrease in pressure in these arteries causes a decrease in uropoiesis. As has already been noted, this effect becomes especially pronounced after preliminary stimulation of renal activity (by injection of physiological solution, hypertonic saline solution, urea solution, etc.). The stimulatory effect of stimulation of the baroreceptors of the sinistral gastroepiploic artery was less pronounced and occasionally inhibited uropoiesis to some extent. An increase in pressure in these arteries is accompanied by an intensification of lymphopoiesis, while a drop in pressure causes a decrease in lymph secretion. The stimulatory effect of stimulation of the baroreceptors of the sinistral gastroepiploic artery is less pronounced and sometimes becomes inhibitory. A rise in pressure in the isolated superior and inferior mesenteric arteries can stimulate or inhibit biligenesis. Shifts between qualitatively different effects are sometimes observed in the same experiment. Finally, changes in pressure in the ureters and urinary bladder may be accompanied by changes in biligenesis and lymphopoiesis. In all these functional reactions of the internal organs, changes in respiration and in the pressure in the common carotid artery, which are produced by the central nervous system, may be lacking. The absence of "true cardiovascular reflexes" in response to physiological stimulation of the baroreceptors of isolated abdominal arteries and the simultaneous presence of so-called conjugate reflexes originating in the abdominal organs forced us to assume that the reactions described can be effected both by central reflex mechanisms and by reflexes originating in the peripheral ganglia.

We have named the vascular receptor areas that, when stimulated, produce limited local reflex reactions "local vascular receptor fields." This designation cannot be interpreted to mean that stimulation of these fields always produces only comparatively restricted local reactions, general reactions (e.g., changes in general blood pressure or respiration) always being absent. General reactions may or may not occur on stimulation of "local receptor fields." This is the principal difference between these fields and the receptor fields of the carotid sinus, aorta, etc., which always produce clear general reflex reactions in blood pressure and respiration when stimulated.

The occurrence of general circulatory reactions on stimulation of "local receptor fields" is undoubtedly due to transmission of excitation from them to the central nervous system, while the absence of such reactions is due to the fact that excitation is transmitted from them to the abdominal and thoracic organs through local, or peripheral reflex arcs. The amplitude and character of the reactions are determined by the specific excitation-transmission conditions in the reflex pathways, the strength of the stimulus, etc. We did not observe these reactions when the pressure in the abdominal veins was raised. This is in all probability due to the fact that veins are equipped primarily with chemoreceptors rather than baroreceptors (O.P. Minut-Sirokhtina and B.Z. Sirotin, 1957). We did not employ chemical stimulation of the veins.

In order to verify the hypothesis that excitation can be transmitted peripherally to the abdominal organs on adequate stimulation of isolated arteries, we conducted experiments involving transection and destruction of the spinal cord at various levels and transection of both vagal sympathetic trunks in the cervical region.

A sharp drop in general arterial pressure undoubtedly has a negative influence on the vital activity of the internal organs, reducing their reflex activity. Nevertheless, the reflex reactions of the internal organs persisted when the pressure in isolated abdominal arteries, the ureters, and the urinary bladder was varied. In such observations consideration need be given only to the altered conditions for general vital activity. Specifically, raising the pressure in the isolated sinistral gastroepiploic artery in the presence of a sharp drop in general arterial pressure after transection of the spinal cord can produce a marked increase in splenic volume. The spleen also enlarges when the pressure in an isolated artery is raised after transection of the spinal cord and against a background of asphyxia, i.e., when central influences tend to cause severe splenic contraction. No special measures to intensify vital activity are required to produce such reactions in the spleen, since the smooth musculature is the effector organ in this case. These reactions can be obtained immediately after transection of the spinal cord, i.e., when spinal reflex activity has been halted by shock.

Our observations of renal activity after transection and isolation of the spinal cord were made under different conditions. Transection and destruction of the spinal cord, which are accompanied by a sharp drop in blood pressure, cause cessation of filtration processes, including those on which uropoiesis is based. After transection of the spinal cord in these experiments it was necessary to await restoration of "automatic" uropoiesis and to inject a substantial amount of physiological solution into the animal's blood stream. The protein pressure of the blood decreased and the difference between its hydrostatic and protein pressures increased. This measure also promoted a rise in arterial pressure. All these factors ultimately led to restoration of automatic uropoiesis and permitted continuation of our observations. It was found that, under these conditions, an increase in pressure in the isolated superior and inferior mesenteric arteries can stimulate secretion of urine by the kidneys. The effect of stimulation of the sinistral gastroepiploic artery was almost always less pronounced and was sometimes inhibitory.

In the latter series of experiments the elapsed time between transection of the spinal cord and restoration of "automatic" or "spontaneous" uropoiesis ranged from 40 min to 2 hr or more; we consequently could not discount the possibility of substantial restoration of the reflex activity of the spinal cord. We were also unable to exclude the possibility that the changes in uropoiesis in response to variations in pressure in the isolated arteries were to some extent due to reflex stimulation effected through the spinal cord. We consequently conducted experiments involving complete and partial destruction of the spinal cord and transection of both vagal sympathetic trunks in the cervical region.

The spinal cord was destroyed by the usual method: the spinal canal was opened at two levels and the cord was withdrawn from its matrix with a flexible probe. Experiments of this type were conducted substantially more frequently than was indicated in the appropriate chapters of this book. We observed the reactions of the urinary bladder and kidneys and the changes in lymphopoiesis and biligenesis. Destruction of the spinal cord was followed by a considerable drop in arterial pressure and we consequently resorted to the same measures as after transection of the spinal cord in order to restore the "spontaneous" activity of the organs and functions under investigation.

Our experiments conclusively demonstrated that there are changes in biligenesis, uropoiesis, and lymphopoiesis when the pressure in the isolated superior and inferior mesenteric arteries is raised after partial or complete destruction of the spinal cord and transection of both vagal sympathetic trunks in the cervical region. On the basis of our observations, we therefore concluded that the changes in the activity of the internal organs (urinary bladder, spleen, kidneys, and liver) and in lymph flow in response to fluctuations in pressure in isolated arteries are due to reflex transmission both through the central nervous system and through local, or peripheral reflex arcs.

What are the characteristics of the reactions effected by peripheral neural mechanisms? Their latent period is a noteworthy feature.

The duration of the reflex reactions of the central nervous system depends on the initial functional state of the reacting element, the strength of the stimulus, the temperature conditions, the recording method, etc. The latent periods of these reactions can consequently range from fractions of a second to several seconds under specific conditions. In A.P. Golovin's experiments, in which one loop of the isolated intestine was subjected to electrical stimulation, the latent period of the reaction of another segment joined to the first by the mesentery was usually 1-2 sec. On adequate uniform stimulation (increases or decreases in pressure) the latent periods of the reactions (isolated pelvic organs, contractions of the bladder and spleen, secretion of urine, bile and lymph) varied rather widely, ranging from several seconds to a minute or more. A long latent period, i.e., delayed onset of the reaction, indicates the presence of considerable resistance in the reaction mechanism. The greatest resistance to conduction of excitation in the reflex arcs of the central nervous system occurs in the synaptic regions. It can consequently be assumed that the principal site of resistance to transmission of excitation in the peripheral mechanism must be the areas of contact between afferent and efferent neurons in the peripheral ganglia. The fluctuations in the duration of the latent periods force us to assume that there is considerable variability in the structure of these contact sites. We will return to this problem somewhat later.

There were substantial after-effects in a large number of observations. Prolonged after-effects were quite clearly seen in our experiments on isolated pelvic and alimentary organs and in our observations of biligenesis and lymphopoiesis. For example, biligenesis can continue at the same level (as during stimulation) for 5 min or more after stimulation of the baroreceptors of the superior mesenteric artery is discontinued. As a rule, the after-effect period is still further prolonged by destruction of the links between the internal organs and the central nervous system. For example, after transection of the spinal cord between the 3rd and 4th thoracic vertebrae in an experiment of 10 May 1951, stimulation of the baroreceptors of the urinary bladder, which causes a decrease in biligenesis and lymphopoiesis, was accompanied by a 15-min after-effect. Prolonged after-effect periods are characteristic of inertial processes.

Substantial after-effects were not noted in the reactions of the urinary bladder and spleen. The reactions were somewhat selective and more or less pronounced. For example, stimulation of the sinistral gastroepiploic artery preferentially induces splenic reactions, reactions of the liver and kidneys being less pronounced or entirely absent. On the other hand, stimulation of the superior and inferior mesenteric arteries produces more marked reactions in uropoiesis, biligenesis, and lymphopoiesis.

Identical stimulation of the baroreceptors of a given artery can induce different reactions (functional excitation and inhibition) in the same organ during a single experiment. Comparison of the effects of stimulation of the superior and inferior mesenteric arteries showed that they vary in extent. The stimuli may be identical in character and strength, but the effect of stimulating the baroreceptors of one artery or the other may be more pronounced. Different reactions were observed during the course of the same experiment. The effects of stimulation on biligenesis and lymphopoiesis were especially variable: inhibitory effects became stimulatory and stimulatory effects became inhibitory. Marked reactions were observed under the action of both weak and strong stimuli.

In order to obtain a sufficiently clear reaction it was sometimes necessary to create a preliminary focus of strong or prolonged stimulation, after which weak stimuli were also effective. In specific cases, strong stimulation thus overcame the inertia of the excitation-transmission mechanism. In many instances there were no reactions when the stimulus strength was slowly increased.

When isolated arteries, the ureters, and the urinary bladder were stimulated with the central nervous system anatomically intact but functionally attenuated, the majority of the biligenetic and lymphopoietic reactions followed the pattern "excitation of one function and inhibition of the other." After destruction of the anatomic links to the central nervous system, equivalent stimuli caused reactions that followed the predominant pattern "simultaneous excitation or inhibition of different functions."

Determination of the mechanism by which the reactions described above are effected is exceptionally important. The following four neural mechanisms can be recognized in peripheral neural regulation.

1. It can be assumed that the peripheral sympathetic nervous system has both a neuronal and a reticular structure. If this is the case, excitation arising at some point in this "network" will propagate throughout the entire "network" and be transmitted through it to the tissues and organs it innervates. However, it is improbable that the reactions described have such a mechanism, since the hypothesis of a syncytial structure for the autonomic nervous system has not been confirmed by histological investigations. B. I. Lavrent'yev, the leading specialist in the morphology of the autonomic nervous system, wrote: "The data amassed since the time of Arnshteyn and Dogel', which have been verified, both by us and by a number of Soviet and foreign laboratories (we should here note our special gratitude for the support given our work by the Kazan' histological school headed by Prof. Mislavskiy,

which has repeatedly checked our data, and the Spanish school of Prof. Ramon y Cajal, especially Prof. de Castro, who has been in constant contact with us), show that there are no grounds for assuming a syncytial structure for the autonomic nervous system. The speculation regarding neural networks is based on an overestimation of modern histological technique, a number of crude artifacts, and a complete neglect of experimentation. The old faults of purely descriptive morphology show up here. Only experimentation, through which we can isolate desired elements of the nervous system and "simplify" its structure, makes it possible to discover previously hidden neural mechanisms in the complex pattern of innervational relationships. Comparative morphology and pathohistology provide strong support in this area. The latter should be an effective method for investigating normal structures, as has been the case in research on the central nervous system."*

We have given so much space to B.I. Lavrent'yev's statements because they show the reason for the erroneous assumption that the autonomic nervous system has a reticular structure and point the way to correct resolution of this problem.

N.G. Kolosov (1948), a leading researcher in the morphology of the autonomic nervous system, wrote that, on the basis of his investigations, he denies any possibility of anastomosis of autonomic nerve fibers such as occurs in Schwann syncytium. The so-called anastomoses between axons in strands of Schwann syncytium described by Buche and certain other researchers are essentially artifacts. N.G. Kolosov (1958, 1961) regards as completely unfounded the conclusion of Meyling and Jabonero (1955) that Dogel' cells of the second type are elements of the network of interstitial cells. The interstitial cells have not been shown to contain neurofibrils or Nissl bodies. This first hypothesis has thus been refuted.

2. Are the reactions described effected by the axon reflexes of sympathetic preganglionic or post-ganglionic efferent fibers? We considered the theory of axon reflexes, particularly the possibility of development of axon-reflex activity in efferent sympathetic fibers, in detail in Chapter 2. In order to again disprove the possibility of axon-reflex activity in efferent sympathetic fibers let us turn our attention to the diagram in Fig. 25.

Figure 25 is a schematic representation of sympathetic ganglia (Sim. uz.), a preganglionic fiber (1) supplying branches to several sympathetic ganglia, a post-ganglionic fiber (2), and internal organs (V.O.).

If the central end of a sympathetic nerve trunk consisting of preganglionic and post-ganglionic fibers is subjected to electrical stimulation, various preganglionic and post-ganglionic sympathetic axon reflexes are regularly and clearly manifested.

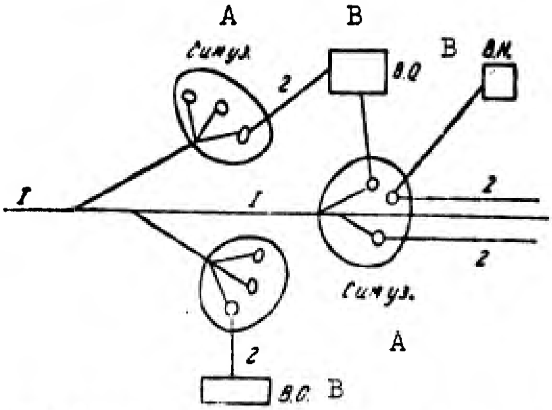


Fig. 25. Diagram of artificial induction of axon reflexes in efferent sympathetic fibers. 1) Preganglionic fiber; 2) post-ganglionic fiber. Sim. uz.) sympathetic ganglion; V.O.) internal organs. A) Sim. uz.; B) V.O.

Belonging to this category are experiments on the relationship between the pigmented cells of the skin and the abdominal organs in fish (Wernoe, 1925), the relationship between the alimentary tract and the heart in the frog (A.V. Tonkikh, 1928), the relationship between the alimentary tract and the heart in warm-blooded animals (A.V. Tonkikh and N.V. Rayeva, 1928; N.F. Popov and A.A. Yushchenko, 1933), the relationship between the anterior extremities and the heart in cats and dogs (A.V. Tonkikh, 1934), et al.

Axon-reflex transmission can be induced in efferent sympathetic fibers when their endings are subjected to direct electrical stimulation. Under these conditions axon-reflexes occur regardless of whether sympathetic or somatic efferent fibers and endings are stimulated.

The situation is totally different if we attempt to visualize the development of axon-reflex activity in efferent fibers under natural conditions. Under natural physiological or pathological conditions the endings of an effector nerve (sympathetic or somatic) can receive excitation only from its fiber and the latter can receive excitation only from the soma of its neuron. This excitation path can never lead to axon-reflex activity. Because of the one-way synaptic conductivity, excitation cannot be transmitted from an effector organ to the nerve endings of an efferent neuron. There has never been any doubt that this is true of the efferent fibers innervating striated muscles. There has never been any doubt that this is true of effector organs innervated by the efferent fibers of the sympathetic nervous system. This fact usually meets with silence when one speaks of the possibility of axon reflexes in the efferent neurons of the sympathetic nervous system under physiological or pathological conditions. Many believe that some sort of exception must be made here, although no proof has ever been advanced. Indeed, there can be no exception, since the sympathetic nervous system has a neuronal structure. One-way synaptic conduction of excitation is as much a basic mechanism for this system as for the motor fibers of the somatic nervous system. If excitation cannot be transmitted from an effector organ to the endings of an efferent fiber, there can be no axon-reflex activity. The one-way conduction of excitation in synapses is a solidly established rule that does not depend on the structural characteristics of the endings of efferent fibers. We consequently assert that the axon reflexes of efferent sympathetic fibers are a phenomenon produced under artificial experimental conditions in physiological laboratories and not one that can occur under natural conditions (physiological or pathological).

The overwhelming majority of our experiments were conducted to study the effect of adequate stimuli – variations in pressure in isolated arteries and organs that generally did not exceed physiological limits. It is indisputable that such stimulation cannot cause excitation to develop in the endings of preganglionic or post-ganglionic fibers or in efferent sympathetic fibers themselves. The reactions of the urinary bladder, spleen, liver, lymphatic system, and isolated pelvic and alimentary organs under our experimental conditions could not have been due to the axon-reflex activity of efferent sympathetic fibers.

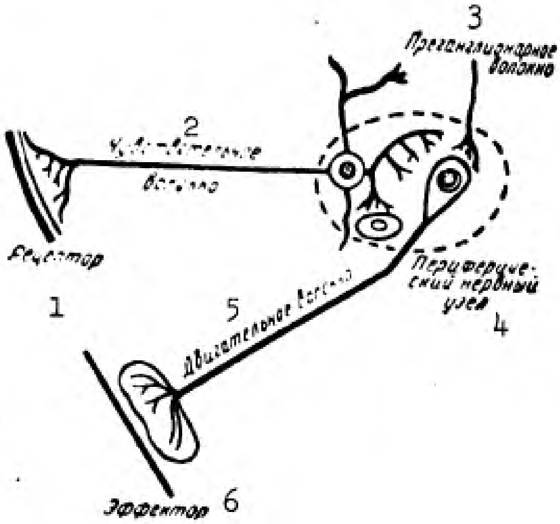


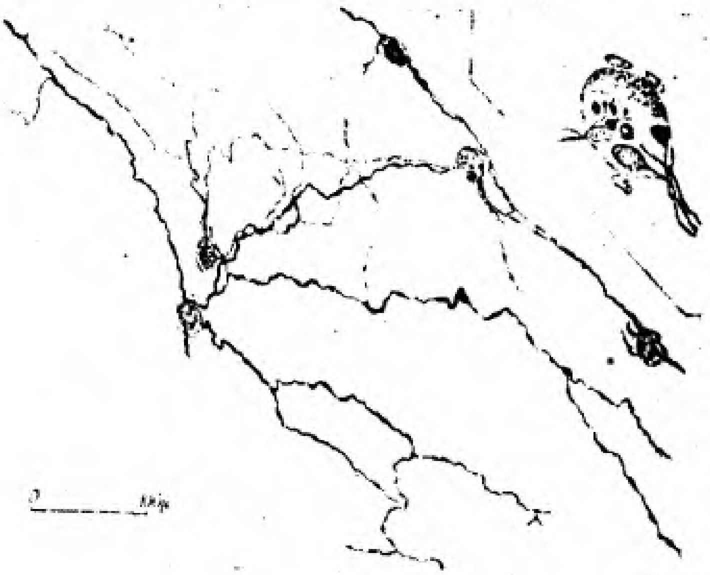
Fig. 26. Diagram of peripheral sympathetic arc. Explanation in text. 1) Receptor; 2) sensory fiber; 3) preganglionic fiber; 4) peripheral ganglion; 5) motor fiber; 6) effector.

Fig. 26a. Sensory nerve cell from Auerbach's plexus of a skate's stomach. Stained with methylene blue.

3. As the third possible mechanism for the reactions described above we must consider local, or peripheral reflex arcs consisting of sympathetic (autonomic) afferent and efferent neurons and completed in peripheral autonomic (sympathetic) ganglia (Fig. 26).

This mechanism is favored by the results of the histological investigations of A.S. Dogel' (1897), I.F. Ivanov (1937), and N.G. Kolosov (1948, 1958, 1961, et al.) and his students (G.A. Koblov, 1951, 1956; A.Ye. Khabarova, 1955, 1960; A.A. Milokhin, 1956, 1958; Yu.I. Slepkov, 1953; et al.), as well as by a substantial number of experimental physiological observations (N.M. Sokovnin, 1877; I.P. Razenkov, 1926; Ye.I. Sinel'nikov and T.P. Gugel'-Morozova, 1937; B.V. Pavlov, 1947; A. Kuntz and C. van Buskirk, 1941; E. Bozler, 1949; I.A. Bulygin, 1957; G.P. Konradi, 1944; et al.).

New morphological data indicating the existence of peripheral reflexes have recently been obtained in N.G. Kolosov's laboratory. A.A. Milokhin (1953, 1958) was able to demonstrate quite clearly that the intramural autonomic plexi of the alimentary tract contain sensory neurons in lower vertebrates (cyclostomes and fish). By way of illustration, Fig. 26a shows a sensory neuron from the gastric Auerbach plexus of a skate (a cartilaginous fish).



GRAPHIC NOT REPRODUCIBLE

Fig. 26b. Synaptic linkage of sensory nerve cells to an efferent autonomic neuron in the intestine of a lamprey. Staining by Bielschowsky-Gross' method.

It can be seen from the figure that the peripheral dendrites of the neuron ramify to form structures whose morphological characteristics (mode of ramification, terminal structure, relationship of termini to surrounding tissues) can only be those of sensory endings.

N.G. Kolosov (1959) made similar observations on mammals. Using cat-intestine preparations, he showed that the peripheral dendrites of Dogel' cells of the second type terminate in brush-like receptor structures. Morphological investigations have thus conclusively demonstrated that the intramural ganglia of the alimentary tract contain true receptor neurons in lower and higher vertebrates. Moreover, A.A. Milokhin

(1953, 1958a, 1958b, 1958c) found that such neurons are synaptically linked to efferent autonomic neurons. He was able to demonstrate the morphological substrate of a peripheral, or local reflex arc (Fig. 26b).*

The figure shows several sensory nerve cells in the intestinal wall of a lamprey. One of these cells was completely stained. Its peripheral dendrites, ramifying into the surrounding tissues, form structures similar to simple brush-like receptors, while its axon runs to the lightly stained efferent neuron and terminates on its soma in typical pericellular (synaptic) apparatuses. As can be seen in Fig. 26b, this same efferent neuron is in synaptic contact with two other sensory nerve cells, showing the phenomenon of convergence so characteristic of the relationship between afferent and efferent neurons.

Figure 26b clearly shows the synaptic linkage between a sensory neuron and an efferent sympathetic neuron, thus being direct proof of the existence of the substrate for a local reflex arc. The whole of this arc, from the receptor in the intestinal wall to the efferent intramural autonomic neuron, can be seen in the preparation.

Many researchers are accustomed to contrast the parasympathetic and sympathetic systems with one another. This opposition is not always warranted, even for the efferent fibers lying in the trunks of these systems. There are no grounds for contrasting the afferent fibers in these systems. There is reason to suppose that both systems contain afferent fibers of the same type rising from Dogel' cells of the second type. They form reflex arcs with efferent neurons in the autonomic peripheral ganglia and can simultaneously transmit excitation from the internal organs to the brain.

4. Another possible mechanism for the peripheral, or local reflex linkage of internal organs is reflex arcs whose afferent elements are

afferent fibers rising from the cells of the intervertebral ganglia and whose efferent elements are the efferent sympathetic neurons of the peripheral autonomic (sympathetic) ganglia. The peripheral ganglia thus serve as the sites of reflex-arc completion in this case as well (Fig. 27).

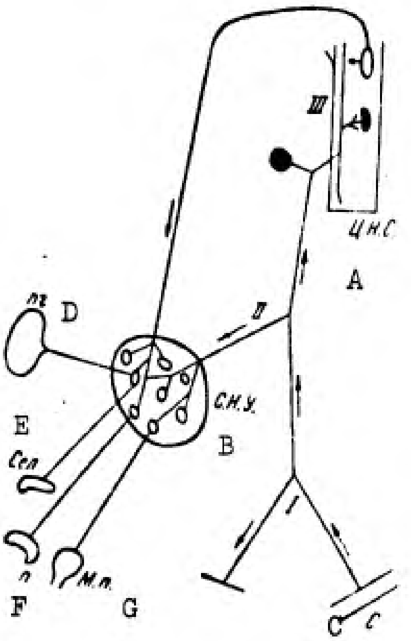


Fig. 27. Diagram of possible transition of neural reactions from axon reflexes of afferent fibers to peripheral reflexes and reflexes of the central nervous system. The reflex arc of the peripheral reflex consists of an afferent spinal neuron and an efferent sympathetic neuron. The arrows indicate the possible propagation of excitation in the afferent neuron as a result of stimulation of its endings in the blood vessel S. I) Path of axon reflex; II) path of peripheral reflex; III) path of reflex of central nervous system. Ts.N.S.) Central nervous system; S.N.U.) sympathethic ganglion; S) blood vessel; pch) liver; Sel.) spleen; p) kidneys; M.p.) urinary bladder. A) Ts.N.S.; B) S.N.U.; C) S; D) pch; E) Sel.; F) p; G) M.p.

We must first call attention to that portion of Fig. 27 which depicts the structure of an afferent neuron. The soma of this neuron lies in an intervertebral ganglion (indicated by the arrows pointing upward). The fiber rising from it ramifies. At the point where it leaves the intervertebral ganglion, one dendrite of the sensory neuron forms two branches. One of these branches runs to the spinal cord and makes contact with new neurons, so that excitation can be transmitted to the effector pathway of a reflex of the central nervous system. The second branch runs to the periphery and terminates in receptors. This branch also divides on its way. The branches rising from it can terminate in various tissues, including the blood vessels (S), the sympathetic ganglia (S.N.U), etc. So-called polyvalent innervation is thus formed. As a result of these structural characteristics of afferent neurons, their functions can vary in the following manner. First, they can effect an axon-reflex type of reaction (Fig. 27, I), e.g., from a blood vessel to the skin and from the skin to blood vessels, etc. This type of reaction is dominant in afferent fibers during the early stages of the development of the nervous system and is the only reaction before the effector neurons have differentiated. Secondly, they can participate in peripheral reflexes (Fig. 27, II). In this case excitation from one of the branches of the fiber, e.g., from a blood vessel (S), is transmitted to the neurons of a sympathetic peripheral ganglion (S.N.U.) and thence along efferent neurons to the effector organs: the urinary bladder (M.P.), the kidneys (p), the spleen (Sel.), and the liver (pch). Thirdly, the afferent neurons of the intervertebral ganglia can also be incorporated into the reflex arcs that effect cerebrospinal reflexes. In this case excitation arising in any of the receptors of the afferent neurons (in the blood vessels, skin, ganglia, etc.) is transmitted to the central branch of the neuron (Fig. 27, III) and thence to the neurons of the central nervous system at any level.

At present, the first type and, to some extent, the first type of reaction in which afferent neurons may participate have been most thoroughly studied. The characteristics of the second type of reaction actually have been given no consideration and have not been studied. Peripheral reflexes and the polyvalency of the endings of afferent intervertebral neurons have been described, but no analysis has been made of the importance of the polyvalency of afferent endings in the mechanism of peripheral reflexes. Special consideration must consequently be given to this problem.

In the second and third types of reactions, i.e., reflex reactions, there are material differences in the structure of the sites of excitation transmission from the afferent to the efferent neuron and there should consequently be differences in the dynamics of excitation transfer from neuron to neuron.

In the second type of reflex reaction the fiber of the afferent neuron ramifies farther from the soma of the cell than in the third type of reaction; this may be reflected in the excitability of the conductive system. In the second type of reflex reaction the endings of the afferent fiber at the sites of interneuronal excitation transmission lie in direct proximity to the somae of the effector neurons, between individual neurons and groups of neurons, as well as in the glia in the connective-tissue membrane of the sympathetic ganglion; they may make contact with the intermediate or efferent neurons of the ganglion.

These characteristics of the location of the sensory endings of intervertebral neurons with respect to the somae of sympathetic neurons in the peripheral ganglia indicate that the transmission of excitation from neuron to neuron occurs under different conditions and requires different stimulus intensities and durations and different excitation characteristics than is the case in the reflex arcs of the central nervous system. Interneuronal excitation transmission should occur at a different rate in the peripheral ganglia. This raises the question of whether the pericellular apparatus is the only form of linkage between neurons. It can be assumed that the pericellular apparatus is the most highly differentiated type of interneuronal linkage, but not the only type. This form of linkage developed as a result of the perfection of the nervous system. The morphological investigations of K.A. Lavrov (1941) and B.A. Dolgo-Saburov (1958) showed that excitation is probably transmitted through unmyelinated axis cylinders by "contact." Pericellular apparatuses are essentially ramified unmyelinated axis cylinders. Ramification, i.e., formation of pericellular structures, increases stimulus efficiency (G.A. Koblov). The accumulation of perifibrilar substance facilitates amplification of neural impluses. Without pericellular structures the transmission of excitation through unmyelinated axis cylinders would be hampered by the low stimulus force. Amplification of the stimulus and prolongation of its action time makes transmission of excitation possible. "... any part of a fiber in contact with the cells to be innervated can be an active site" (K.A. Lavrov, 1941).

A probable excitation-transmission mechanism involves the participation of "special" cell having a common origin with the glia but differing from it morphologically and, possibly, functionally. These cells should be extremely sensitive to chemical stimuli, as has been confirmed by the investigations of I.A. Bulygin and his colleagues (1962). The presence of enzymes may facilitate excitation transmission (V.V. Portugalov, 1955). We cannot exclude the possibility that an intermediate linkage can be effected by the argentophilic base substance, the reticular fibers of the loose connective tissue (S.M. Milenkov).

A characteristic consequence of the functional characteristics of any of the linkage mechanisms suggested is retarded excitation transmission. This is in complete agreement with the results of our observations. The latent periods of the reactions described are always quite long, ranging from several seconds to several minutes. These reactions require comparatively long stimulation times and, occasionally, strong preliminary stimulation. The prolonged after-effect periods indicate the low functional lability of the sites of interneuronal excitation transmission in the peripheral ganglia.

It is quite possible that the prolonged latent periods and after-effect periods are due to the fact that chemical substances with substantial physiological activity are formed at the sites of interneuronal excitation transfer under the influence of stimulation and then accumulate metabolically. These substances increase the excitability of the efferent sympathetic neurons and thus facilitate excitation transmission. This agrees well with the fact that creation of a focus of prolonged or strong stimulation is sometimes necessary to produce a reaction.

The reactions we have described can thus be effected by two reflex mechanisms. While the afferent and efferent components of one reflex arc are completely sympathetic (autonomic) in origin, the afferent portion of the other consists of an intervertebral neuron exhibiting axon-reflex activity and its efferent portion consists of efferent sympathetic neurons. In both cases the reflex arcs are completed in sympathetic (autonomic) peripheral ganglia. These reflex mechanisms are not mutually exclusive, but supplement one another, thus making the peripheral neural regulation of tissue and organ activity more diverse. The concept of a purely sympathetic peripheral arc is based on the investigations of N.G. Kolosov and his colleagues. The concept of a peripheral arc consisting of an efferent spinal neuron and an efferent sympathetic neuron is based on the histological investigations of V.I. Lavrent'yev and A.A. Milokhin (1959) and others.

There arises the question of whether the reactions we have described result exclusively from the axon-reflex activity of afferent neurons, without transmission of excitation to efferent sympathetic neurons. There is no doubt that afferent neurons can exhibit axon-reflex activity under natural conditions. However, the overwhelming majority of the reactions described cannot be attributed to the axon-reflex mechanism of afferent fibers in its "pure" form.

The reactions described have a rather wide "field," i.e., a broad specific distribution. Because of the comparatively limited ability of afferent fibers to ramify, their axon reflexes cannot have a wide distribution.

Their conformity to the three conditions laid down by V.N. Chernigovskiy (1944) indicates that the reactions described are based on peripheral reflex arcs: 1) the reactions persist after destruction of the central nervous system; 2) adequate stimulation was employed to induce them; 3) interaction of the basic nervous processes, excitation and inhibition was observed during the reactions.

A few remarks must be made about the classification of peripheral reflexes. The concepts of "peripheral" and "local" reflexes are identical and the reflex arcs involved are completed in the peripheral autonomic ganglia in one of the two ways described above. Peripheral, or local reflexes must be subdivided into two groups in accordance with the location of the ganglia in which the reflex arcs are completed: intraorganic (intramural) and interorganic (extramural). Interorganic peripheral reflexes are in turn subdivided into intrinsic (within a single functional system) and intersystemic reflexes. This is the classification we recommend for peripheral, or local reflexes.

Comparison of the physiological characteristics of the axon reflexes of afferent neurons, peripheral reflexes, and the reflexes effected by the central nervous system leads us to conclude that the "field," complexity, and variability of the reactions increases as we move from the first type of neural regulation to the second and third types. The axon-reflex reactions of afferent neurons are always more limited in spatial distribution than peripheral reflexes. The entire body may actually be involved in the reflex reactions of the central nervous system, but, as a result of the complex interaction of neural processes, they appear to be spatially quite distinct in each specific case. The regulatory significance of the nervous system thus varies. From a local regulatory mechanism (the axon reflex of an afferent fiber is a mechanism of limited extent and a peripheral reflex is one of greater extent) the nervous system becomes a unified mechanism for regulating the body's vital activity.

As reactions effected by the nervous system, the axon reflexes of afferent fibers are extremely simple and comparatively invariant. Peripheral reflexes are a simpler form of reflex activity than the reflexes of the central nervous system, but are based on the same mechanisms, including summation, inhibition, pathway formation, quantitative and qualitative modification of reflex reactions, interaction of reflexes, mutual induction, etc. Peripheral reflexes are the mechanisms for the primary neural autoregulation of the internal organs.

It would, however, be a grave error to regard the peripheral reflexes of animals, including the higher vertebrates, as something independent and isolated. The structural characteristics of their reflex arcs make this impossible. Throughout the autonomic ganglia in which peripheral reflexes are completed are the endings of fibers from the intervertebral neurons, through which signals regarding changes in the gangliar nerve cells are transmitted to the central nervous system. In turn, afferent fibers run from the central nervous system to the peripheral ganglia. This interaction mechanism can be present regardless of the structure of the peripheral reflex arc. When a peripheral arc consists of an afferent intervertebral neuron and an efferent sympathetic fiber, the same afferent neuron is incorporated into the peripheral arc and an arc completed at some level of the central nervous system. The interactions produced are of the same type as those between reflexes completed at the level of the spinal cord, myelencephalon, cortex, etc. As I.M. Sechenov (1891) showed, in such cases cerebral reflexes are dominant under physiological conditions.

Under natural conditions, the peripheral reflexes of higher animals are a link in the neuroregulatory chain, in which the cerebral cortex is of prime importance. The internal unity of the body and its unity with the environment result from regulatory mechanisms modified during evolution. As the structure and activity of the organism become more complicated, its regulatory mechanisms become more complex and more advanced.

According to I.P. Pavlov, regulation is based on the interaction of reflex processes and the transition from lower to higher forms of nervous activity, which may occur over a short period of time and thus permits individual adaptation to changes in the environment. New forms of reflex reactions have also developed during evolution. New, progressive reflex reactions have been produced and fixed by morphological reorganization of the nervous system over a number of generations. The nervous system of primitive animals (cephalopods) becomes a gangliar system (molluscs), then a segmented system (arthropods), etc. Because of their incompleteness, current data on the principal stages of the development of the nervous system are of only relative value. It is possible that the developmental stages in chordates and their ancestors (echinoderms, chaetognaths and coelenterates) had their own special features. There is no doubt that the nervous system has become more complex and advanced in structure and function during its evolution from its primitive form.

It is still widely supposed that newer forms of regulatory mechanisms appear during evolution as a supplement to older forms, the latter being suppressed rather than eliminated by the former. With the development of newer forms of regulation the older forms pass into a latent, "somnolent" state. They can be roused from this state if the newer forms cease to function.

It is obvious that the development of new forms of regulation is completely detached from the old forms in this interpretation of the formation and action of regulatory mechanisms. The latter are depicted as separate stages rather than as a monolithic whole, all lower elements of the nervous system having their activity suppressed or inhibited. This notion inevitably leads to the conclusion that the higher elements of the brain are the sole regulatory apparatus in the higher warm-blooded animals, including man, and that the remainder of the central and peripheral nervous systems consists of "suppressed" elements essentially not needed for normal vital activity. From this standpoint, only a humoral regulatory mechanism can have a two-fold action, i.e., peripheral and central.

In this interpretation of the evolution of regulatory mechanisms physiological processes are separated from pathological processes. The latter are regarded as the result of "structural accidents" in new forms of regulation and the appearance of older forms. The process of evolution is considered from the standpoint of quantitative accumulation of philogenetically "new" centers and not of qualitative modification of all neural activity. Past stages in the evolution of neural regulation are reactivated as soon as these new centers are disrupted.

We feel another theory to be correct: this holds that the progressive development of the nervous system does not culminate in the appearance of some new, higher-order center. When new structural and functional forms are established and fixed during adaptation the process that takes place is not formation of a higher-order center but qualitative reorganization of the entire regulatory function of the neural apparatus. New relationships and connections develop between the nerve centers. The old regulatory structures naturally cannot become something "in reserve" or "somnolent." They are completely eliminated if the induction of new, progressive forms of adaptation is impeded or, losing their original characteristics, e.g., the ability to function autonomously, acquire new ones and are incorporated into the newly formed regulatory mechanisms.

New forms of regulation thus encompass old forms, transforming them into an integrated system. The development of the nervous system and the perfection of new, progressive properties occurred by both elimination and improvement of old properties. In such a nervous system the interaction of reflexes at certain points in vital activity may produce reactions effected by different elements of the system, including the peripheral sympathetic (autonomic) ganglia. We regard the appearance of peripheral reflexes in warm-blooded animals under normal conditions, without preliminary isolation of the central nervous system, as being the result of a complex interaction encompassing the entire nervous system, primarily its sensory portion. The possibility of such manifestation of the activity of one element of the complex neural mechanism of functional regulation not only does not detract from the prime importance of the higher portions of the brain, but actually results from it, if only by virtue of the fact that these regions constantly receive signals pertaining to the activity of lower elements of the nervous system, as well as because peripheral and central reflexes can share the same afferent neurons.

Transection or destruction of the spinal cord, transection of both vagal sympathetic trunks in the cervical region, or any other disengagement of the central nervous system cannot cause previously eliminated forms of neural activity to reappear.

It is known that isolation of the higher regions of the central nervous system leads to changes in its lower regions, the visible manifestations of these alterations being nonuniform. In certain cases such isolation causes temporary depression of the activity of the lower elements or complete cessation of a given function. In other, quite definite instances, isolation of the higher regions of the nervous system leads to immediate or delayed intensification of certain functions, to the appearance of reactions which are absent under normal conditions but were present at a definite stage in the development of the nervous system.

How are we to interpret the development of these changes?

The depression and cessation of functional activity can be explained in the following manner. A function disappears because the principal element of the neural apparatus regulating it, the appropriate nerve center, has been completely destroyed. Functional depression results from shock. The intensification of a given function after partial isolation of the nervous system is due to the elimination if inhibitory influences. The classic example of this is the acceleration of cardiac activity in mature dogs after transection of both vagus nerves.

Some researchers attribute the appearance of reactions that were absent before destruction of the higher elements of the nervous system but existed at a definite stage of the development of this system to restoration of older forms of regulation that had disappeared during evolution.

This explanation naturally cannot stand up to criticism, since that which disappeared as a result of evolution cannot reappear. If a given reaction is manifested, this means that it could have appeared when the nervous system was intact. The appropriate mechanism existed, but was incorporated into a more complex regulatory mechanism. Transection of the spinal cord does not cause formation of something that was previously absent, but demonstrates the results of simplification of the regulatory apparatus, making manifest the activity of its individual elements under new conditions. In our opinion, the clearer manifestation of peripheral reflexes after destruction of the links between the internal organs and the central nervous system results from simplification of the regulatory apparatus and not from simple deinhibition of some higher center. The interactions within the remainder of the neural apparatus become less complex and the reactions it effects are consequently less complex than those carried out by the entire central nervous system; they are nevertheless typical reflex reactions.

On the basis of our investigations we can make the following generalizations.

1. We have cited a number of experimental and theoretical proofs of the existence of peripheral reflexes completed in the peripheral sympathetic (autonomic) ganglia of vertebrates, including the higher vertebrates. There are two structural variants of such reflex arcs. One type of arc consists of an afferent neuron whose soma lies in an intervertebral ganglion and an efferent sympathetic neuron. The other type of arc consists of afferent and efferent neurons of sympathetic (autonomic) origin.

In both cases the peripheral reflex arcs are completed in peripheral sympathetic (autonomic) ganglia.

2. The concepts of "local" and "peripheral" reflexes are identical. They mean the same thing: the reflex arcs of local, or peripheral reflexes are completed in the peripheral ganglia and reflex reactions

can be effected without participation of the central nervous system. Peripheral reflexes are subdivided into two groups in accordance with the location at which their arcs are completed: intraorganic (intramural) and interorganic (extramural). Interorganic peripheral, or local reflexes must be subdivided into "intrinsic" reflexes, in which the afferent and efferent neurons that effect the reflex originate and terminate in the same functional system, and intersystemic reflexes, in which the afferent neurons originate in one functional system (e.g., the vascular system), while the efferent neurons terminate in another system (e.g., the urinary, digestive, or some other system).

3. Our observations showed that the intraorganic and intrasystemic peripheral reflexes of the alimentary system can easily be detected by employing adequate stimuli (increases in pressure). These conditions also make it easy to observe intersystemic reflexes with arcs whose afferent neurons originate in the vascular or urinary system and whose efferent neurons terminate in the alimentary, lymphatic, or urinary system or the spleen. It is substantially more difficult to detect intersystemic peripheral reflexes originating in the alimentary organs and terminating in the heart.

4. Peripheral reflexes are one of the lower forms of reflex regulation. The structures that effect peripheral reflexes in the higher vertebrates are not independent, i.e., are not isolated anatomically or functionally from the reflex structures of the central nervous system. They are incorporated into new forms of regulation, in which the brain is of prime importance. This is demonstrated by the structural and functional characteristics of peripheral reflex arcs. The entire regulatory apparatus, with all its interacting elements, is an integrated unit and its reactions are effected by various elements, including peripheral reflex arcs, in accordance with specific functional

conditions.

5. Under natural physiological conditions, peripheral reflexes are the result of interactions throughout the entire regulatory apparatus. When the links between the internal organs and the central nervous system are anatomically disrupted, i.e., under pathological conditions, the peripheral reflex apparatus may assume full responsibility (in conjunction with humoral factors) for regulating the vital activity of the internal organs to which it is connected.

6. When the links between the internal organs and the central nervous system are intact, peripheral intersystemic reflexes of the "abdominal vessels to abdominal organs" type occur against a background of constant respiration and constant arterial pressure in the systemic circulatory system, following the dominant pattern "simultaneous excitation of one function and inhibition of the other." After complete destruction of the neural links between the internal organs and the central nervous system, these reflexes follow the dominant pattern "simultaneous excitation or inhibition of different functions."

7. Peripheral reflexes have prolonged latent and after-effect periods, which indicates that the processes taking place in their reflex arcs possess inertia. The reaction field exhibits a definite selectivity. For example, when the sinistral gastroepiploic artery is stimulated the most pronounced reaction is in the spleen; on the other hand, when the mesenteric arteries are stimulated the most pronounced reactions are in the urinary bladder (inferior mesenteric artery), kidneys, liver, and lymph vessels.

8. Peripheral reflex reactions are rather diverse in character. Adequate stimulation of the vascular receptors or the receptors of the bladder and ureters sometimes causes both excitation and inhibition of the activity of the internal organs. Under specific conditions it can

be seen that adequate stimulation of the receptors of one artery has a predominantly stimulatory effect on a given function, while stimulation of the receptors of another vessel inhibits this function. Stimulatory and inhibitory effects may alternate during a single experiment, even when the same angioreceptors are subjected to adequate stimulation.

9. The so-called axon reflexes of efferent sympathetic fibers are an artificial product of experimentation in the physiology laboratory and not a phenomenon that can arise under natural conditions (physiological or parthological).

10. The axon reflexes of afferent nerve fibers are undoubtedly of physiological importance; these reflexes may be constituents of peripheral reflexes, since the ramified fibers of an afferent neuron may be incorporated into a peripheral reflex arc.

Manuscript Page No.	[Footnotes]
166	B.I. Lavrent'yev. Morfologiya avtonomnoy nervnoy sistemy [Morphology of the Autonomic Nervous System], 1946, page 77.
172	We express our heartfelt gratitude to A.A. Milokhin, who generously contributed Figs. 26a and 26b.

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