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THE VENOPRESSOR MECHANISM

By Professor YANDELL HENDERSON

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"WE have yet to explain in what manner the blood finds its way back to the heart from the extremities by the veins." So wrote William Harvey:[1] and now 300 years later the explanation is still not wholly complete. As a major factor in the venous return, Harvey described the valves in the veins and showed, by moving a finger along a vein in the arm, that "while these valves readily open in the right direction," *i.e.*, toward the heart, they "entirely prevent all contrary motion." And he accompanied the description with a drawing, copied from Fabricius,[2] showing a man's forearm with a ligature above the elbow and the hand grasping a rod, while the veins swell. In the grip of the hand in that drawing is the first suggestion of a venopressor mechanism.

It is always dangerous to read subsequent knowledge back into the words of the first author in any field. Yet one can not resist the impression that Harvey, in this drawing along with his account of the valves in the veins, recognized that the vigorous contraction of the muscles of the forearm propels blood from the muscles into the veins and on toward the right heart. If so, he would have been entirely in accord with the modern view that any muscle that is rhythmically relaxed and contracted, so that its capillaries are alternately filled from the arteries and emptied into the veins, acts as a peripheral pump, a "booster,"[3]

[1] W. Harvey, "The Motion of the Heart and Blood in Animals." London, 1628. Chap. 13. Everyman's Library, New York, 1906. Also translation by C. D. Leake, published by C C Thomas, 1931.

[2] H. Fabricius, "DeVenarum Ostiolis," 1603. Translation by K. J. Franklin, published by C. C Thomas, 1933, pp. 80, 81.

[3] Booster: A pump used to increase the pressure of

aiding the venous return of the blood and the diastolic filling of the heart.[4]

How well the intramuscular blood vessels are arranged to act the part of such peripheral blood pumps is clearly described by Krogh.[5] He writes:

> The arteries supplying a muscle branch freely and between the branches there are very numerous anastomoses forming a primary net. . . . The capillaries unite into venules intercalated between the arterioles, and the whole system of veins reproduces and follows almost exactly that of the arteries. All the veins down to the smallest branches are provided with valves allowing the blood to flow in the direction of the heart only. When the muscle contracts its form is greatly altered, the fibers become much shorter and proportionally thicker, . . . The blood is driven out by compression from a number of the venous branches and, when the muscle relaxes again, these can be filled from the peripheral end only. Since muscular contractions usually more or less regularly alternate with relaxations the system of valves makes of the veins of each muscle a very effective pump. . . .

So the muscles provide a venopressor mechanism to meet the increased demands on the circulation which the muscles themselves create during periods of physical exertion. There can be little doubt that it is largely by such peripheral aid to the venous return that the enormous increase in the output of the heart—at least five fold—during vigorous muscular exertion is made possible.

But suppose the exertion ceases and the man stands quite still, or sits down, or lies down and rests so completely that for a time no muscle in his body makes any visible movement, or does any external work. Does the pumping action of the muscles cease entirely? Is the venous return then wholly dependent upon the vis a tergo imparted by the heart and transmitted through the arteries and capillaries into the veins, and so onward to fill and distend the right heart? In other words, to paraphrase Harvey's question, "could the blood find its way back to the heart from the extremities by the veins" without some peripheral aid? There is strong evidence that it does not, and that it could not; but that at least in health there is constantly active peripheral aid to the venous return. It is only in the state called shock and other conditions of profound physical depression that this booster action fails. The testimony now to be cited indicates that even in the most complete state of healthy rest and quiescence the muscles are still pumping and that the venopressor mechanism, as above described, is still active so long as the motor centers in the spinal cord continue to discharge nervous impulses into the skeletal muscles in the maintenance of tonus.

Muscle Tonus and its Control

Sherrington,[6] in his classic analysis of the proprioceptive reflexes by which muscle tonus, body posture and facial expression—and to a considerable extent also basal metabolism—are maintained and adjusted, showed decisively that even when the body is at rest, and appears to be entirely motionless, the skeletal musculature is far from flaccid. On the contrary, as he expressed it, "the greater part of the skeletal musculature is all the time steadily active."

More recent studies, such as those of Adrian[7] and Adrian and Bronk[8] on single nerve fibers, have confirmed the conception that the mode of behavior of all the nerve-muscle mechanisms involved in external motion and active work holds equally true of the tonic contractions of the muscles that maintain posture even in normal rest. Between the states of bodily exertion and muscular rest, apparently so different, the form of activity within the muscles is exactly the same: varying only in degree.

In the so-called "isometric contractions," that tonus maintains when a man is standing or sitting, and even when lying down, the muscles do not shorten and do no external work. They do, however, exert an elastic pull to maintain posture. A weak pull of this type, which for lack of a better term is here called tonus, is due to impulses from motor centers in the spinal cord over only a few nerve fibers which induce contractions only in correspondingly few bundles of muscle fibers; but the impulses over each of these nerve fibers and the contractions, or elastic pulls, of each of the bundles so stimulated are maximal. A stronger pull of the muscle is due to impulses over a greater number of nerve fibers and a more rapid succession of impulses in each fiber, which stimulate a greater number of bundles of muscle fibers: the bundles contracting, or pulling, not all together, but in relays and rotation.

Contrariwise, as the activity of a muscle decreases to lower and lower degrees of intensity, until it is apparently wholly quiescent and doing no external work whatever, nervous impulses pass over fewer and fewer nerve fibers from the motor centers, and fewer and fewer groups of muscle fibers are at any instant active. Yet it appears probable that no living muscle is ever allowed to cease its tonic pull completely.

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fluids. Webster's New International Dictionary. Second Edition. Unabridged, 1934.

[4] Y. Henderson, "Adventures in Respiration." Williams and Wilkins Company, 1938.

[5] A. Krogh, "The Anatomy and Physiology of Capillaries," p. 208. Revised edition. Yale University Press, 1929.

[6] C. S. Sherrington, "The Integrative Action of the Nervous System," p. 340. Charles Scribner's Sons (for Yale University) 1906.

[7] E. D. Adrian, "The Mechanism of Nervous Action." University of Pennsylvania Press, 1935.

[8] E. D. Adrian and D. W. Bronk, *Jour. Physiol.*, 67: 119, 1929.

Always a few of the motor nerve fibers to it are discharging impulses into it, and a few of its bundles of muscle fibers are stimulated to contract.

Such, as nearly as the picture can be constructed from the experimental data now available, is the state of continual internal activity which is skeletal muscle tonus. It is a state which no part of the body loses completely except at death. So long as it is maintained it involves continuance of the pumping action of the discrete muscle bundles relaxing and contracting one after the other and thereby filling, compressing and emptying their intercalated capillaries and veins in the manner that Krogh[5] has described for the muscle as a whole.

The action of these minute pumps is the principal, but not the only, aid that muscle tonus affords to the venous return. A longitudinal pull on such a structure as a muscle necessarily induces a general internal pressure; and a pressure anywhere in a system permeated with collapsible vessels containing a fluid tends to cause the fluid to flow toward any point where the pressure is lower. That is the basic conception of hydraulics and hemodynamics. If, then, the state of tonus in muscles maintains an intramuscular pressure higher than that of the atmosphere about the body, and the pressure in the thorax is subatmospheric—the two pressures together constituting the effective venous pressure—the tonic intramuscular pressure must aid the venous return that distends the right ventricle. That such intratissue pressures do normally exist is now demonstrated by a considerable literature.[9] They are measured by determining the pressures required to force a minute amount of a saline solution through a hypodermic needle into a muscle or other tissue; and the pressures so demonstrated are found to vary according to the tension on the muscles: that is, their tonus. By maintaining pressures upon other tissues, as in the abdomen, muscle tonus conserves in the capillary blood some of the energy that the heart has imparted and tends to press onward toward the veins the blood which the arterioles throw into them.

The Electromyogram

Every time that a muscle fiber contracts it manifests its activity by an electrical event, the so-called action current. If, then, a muscle such as the biceps in a man's arm containing hundreds of separate muscle bundles is maintained in a state of tonus, the number of bundles that are thrown into contraction at any instant should be revealed in the electromyogram. In other words, the number of electrical impulses appearing in such a graphic record should indicate the number of minute capillary and venule pumps that are making discharges toward the heart. If this is correct, a series of such electromyographic records made at times when the biceps is entirely immobile externally, but under different degrees of tension, should show varying degrees of electrical activity corresponding to the degrees of tension. Accordingly, at my request, my colleagues of the Section of Neuro-Anatomy have recorded the series of electromyograms which are here reproduced. They reveal that the biceps of a man lying at rest with his arm relaxed, as in the first record, or perfectly quiescent under slight strain, as in the other records, is "all the time steadily active." They show that the number of bundles of muscle fibers in a muscle that are nervously activated varies with the intensity of the longitudinal pull that the muscle maintains. And the same evidence, interpreted in accord with Krogh's description, indicates that the number of minute pumps that are actively aiding the venous return to the heart varies correspondingly.

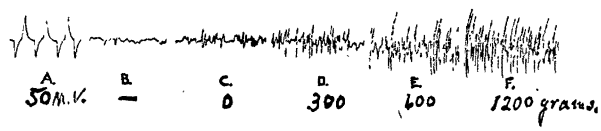

FIG. 1. Showing graphic records of the electromyogram of the biceps brachii under increasing tension: *i.e.*, the electrical discharges accompanying the contractions of an increasing number of muscle bundles and the corresponding strokes of the capillary-venous booster pumps. (A) Calibration, 50 micro volts. (B) Subject lying supine, arm beside body, biceps "at rest." (C) Biceps contracted sufficiently to hold the elbow flexed at 15 degrees. (D) Same position, 300 gram weight in hand. (E) Same position, 600 gram weight in hand. (F) Same position, 1200 gram weight in hand. Arm perfectly quiescent during the taking of each record. Records by courtesy of the Section on Neuro-Anatomy. (Graph by L. F. Nims.)

The Tonic Activity of the Motor Centers

Skeletal muscles have little intrinsic activity. Unlike cardiac muscle their behavior is imposed upon them from the central nervous system. To trace the various influences that act upon the accessory blood pumps in the muscles, we must therefore look behind the muscles to the motor centers in the spinal cord which innervate them. Yet it is only by the behavior of the muscles that we can judge how various influences affect the state of their motor centers.

As the means of testing that state two types of experiments are available. One is by means of what Sherrington has termed "proprioceptor reflexes," of which the most convenient is the knee jerk. For this

[9] Y. Henderson, *loc. cit.*, p. 243; also J. D. Kerr and L. D. W. Scott, *Brit. Med. Jour.*, 2: 758, 1938; W. Beigelbock and H. Jung, *Zeitschr. f. klin. Med.*, 131: 242, 1937; H. S. Wells and H. S. Youmans and D. G. Miller, Jr., *Jour. Clin. Invest.*, 17: 489, 1938; F. A. Hillebrandt, E. J. Crigler and L. E. A. Kelso, *Am. Jour. Physiol.*, 126: 247, 1939.

purpose the thigh must be supported and fixed in an unchanging position and the taps on the patella tendon must be applied at uniform intervals by a light hammer falling through a uniform distance. With this arrangement it has been found that virtually any and all events anywhere in the body affect the knee jerk either to an increase or decrease: inspiration, expiration, clenching a hand, mental arithmetic, somnolence, a sudden loud sound, and so on almost endlessly are such influences. In the present connection, the most significant influence upon the motor centers is, however, chemical: the influence of the blood gases. Thus as Henderson, with the collaboration of Coffey and Barnum,[10] found, a period of forced overbreathing sufficient to induce a slight acapnia (deficiency of carbon dioxide in the blood) and a subsequent brief period of failure of breathing, was followed also, for a slightly longer time, by the abolition of the knee jerk also. Contrariwise rebreathing from a small bag, until enough carbon dioxide had accumulated in the blood to induce a slight increase in the volume of breathing, induced a marked augmentation of the knee jerk. These facts suggest strongly that the blood gases, particularly carbon dioxide, exert an influence upon motor nerve centers that is manifested in muscle tension and the activity of the intramuscular booster pumps essentially as the blood gases are known to influence respiration. In other words, under ordinary normal conditions the amount of carbon dioxide produced in the body determines both the volume of air breathed and the volume of blood circulated. In this way, as Miescher[11] first recognized, the oxygen supply of the body is safeguarded by carbon dioxide.

The other experimental method by which it is possible to test the state of motor centers in their control of muscle tonus has more recently been employed by Henderson and Turner[12] in their study of artificial respiration. They have shown that it is the "elasticity" of the thoracic muscles and diaphragm which makes artificial respiration possible; that this feature of these and other muscles is not a mere mechanical elasticity, but a vital property due to tonus under nervous control; and that in a normal man under artificial respiration it is the blood gases acting upon the respiratory center and its subordinate motor centers that determine the degree of tonic elasticity in the muscles that they innervate. These findings, which are in general accord with those of Hess[13] in experiments on animals, are of particular interest in view of the campaign for the teaching of First Aid by the American Red Cross just now, as this teaching includes the Schafer prone pressure method of artificial respiration. Evidence both in the laboratory and in cases of drowning, electric shock and carbon monoxide asphyxiation indicates that inhalation of a mixture of carbon dioxide and oxygen by increasing the tonic elasticity of the respiratory muscles is a valuable aid to manual artificial respiration in essentially the same way that it increases natural breathing. Both types of evidence show also that such devices as pulmotors, resuscitators, and other suck and blow apparatus are highly unphysiological and may actually do harm. An even greater practical objection to such mechanical devices is that they take time to apply and thereby delay the all important immediate application of artificial respiration. As tonus quickly fails in cases of asphyxia, drowning and electric shock, a delay of a few seconds often causes the loss of a life.

[10] Y. Henderson, *Am. Jour. Physiol.*, 25: 310, 1910.

[11] F. Miescher, *Arch. f. Anat. u. Physiol.* Physiol. Abth., 1885, p. 355.

[12] Y. Henderson and J. McC. Turner, *Jour. Am. Med. Asn.*, 116: 1508, 1941.

[13] W. R. Hess, "Die Regulierung der Atmung." Georg Thieme, Leipzig, 1931.

Peripheral Circulatory Failure and Asphyxia

Whenever, as a consequence of acute illness or physical injury and pain, some of the centers in the nervous system break down and fail in their normal function, one of the accompanying manifestations is a failure also of the circulation. The nervous failure was formerly assumed to be primarily in the vasomotor centers, and to induce a relaxation of the peripheral blood vessels. To that conception the venopressor mechanism now affords an alternative. But no matter whether the primary failure is in the vasomotor control over the arteries and arterioles with pooling in the splanchnic area, as heretofore believed; or whether, instead, the failure is in the spinal motor centers with loss of muscle tonus and slowing of the blood stream in the flaccid muscles, as here presented, the result is the same: a slowing of the blood stream.

Given a progressive slowing of the blood stream leading to peripheral circulatory failure and the first stage of shock, the next problem is that of how the second stage develops from it: that stage consisting in a decrease of blood volume which further diminishes the venous return and the minute-volume of the circulation.

In health the blood stream is so large, or rather so rapid, that in each minute it brings to the tissues a large excess of oxygen; and the excess goes on into the venous blood. When, however, in the development of shock or in the prostration of acute disease, the venopressor mechanism gradually fails, the venous return grows less and less, the circulation progressively slower and slower. Consequently the excess of oxygen brought to the tissues becomes smaller and smaller, until none is left to pass on into the venous blood. The arterial blood is still fully loaded with

oxygen, but as the volume-flow decreases a point is finally reached at which the demands of the tissues are no longer met.[14] Tissue asphyxia then develops, and with it a process analogous to edema. The walls of the capillaries become permeable;[15] and the serum of the blood and some corpuscles ooze out into the tissues. Three interacting results follow: oligemia, bradyrhea,[16] and asphyxia: *i.e.,* decrease of blood volume, slower and slower flow of blood through the tissues and finally anoxia of the tissues.

Such appears to be the causal sequence through which failure of the tonic activity of the motor centers initiates the development of shock. That this sequence is essentially correct is confirmed by the benefit which is now obtained from the intravenous administration of serum. In shock, if accompanied by little or no hemorrhage, the red corpuscles, which are the oxygen carrying portion of the blood, are still in the body, but stagnant, and need only serum to float them. The benefit afforded by mere serum in shock serves to distinguish shock from hemorrhage; for serum alone, even when reinforced by inhalation of oxygen, as it should be, can transport little oxygen. After an exsanguinating hemorrhage, on the contrary, the essential and only means of saving life is restoration of at least some part of the red corpuscles by infusion of whole blood.

Similar in appearance as are the effects of extreme hemorrhage to those of shock from venopressor failure, hemorrhage[17] has an even closer fundamental likeness to carbon monoxide asphyxia, in which the corpuscles are deprived of their capacity to transport oxygen. Yet in their final stages, hemorrhage and shock are as truly forms of asphyxia as is the tissue anoxia induced by carbon monoxide. In all three conditions, the fundamental need is oxygen;[4,18] but the best method of restoring the supply of oxygen in each is different.

Estimation of the Venous Return

Solution of the problems of circulatory failure has been greatly retarded by the lack of a simple method for estimating the volume of the venous return in health and disease. Under just those conditions of failing vitality in which it is most important to follow the decrease or recovery of the venous return, venous pressure is often immeasurably low. It has, however, been found[19] that significant measurements can be made quite easily when the body is inverted at least to such a degree—a slope of 1:4—that all the blood returning from the tissues is—so to speak—poured into the great veins near the heart: the preventricular reservoir of von Recklinghausen. Although this head-down position is not so much of an aid to the circulation as surgeons generally believe, it is of great value for diagnosis. For when one of the patient's arms is then held vertically, or lifted gradually, the top of the column of blood in the veins usually shows a sharply defined meniscus, and the height of that column above some point of reference, such as the symphysis of the clavicles, affords an index of the volume of the venous return. Estimated in this way that volume has been found to be greatly decreased after some major surgical operations and in cases of acute illness. As recovery develops the venous column rises again; as vitality fails, the column sinks progressively lower until it reaches zero as the tonus of the body's musculature disappears at death.

MILITARY GEOLOGY FROM THE AIR

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THIS paper is written to call attention to the existence of a small body of men competent to perform a new and unique service in the war effort—the interpretation and mapping of geological information of military value revealed on aerial photographs.

The present war, with theaters of activity in regions little known and poorly mapped or entirely unmapped, many of them in enemy hands and inaccessible for study on the ground in advance of occupation, makes it necessary to depend almost entirely on aerial photographs for both topographic and geologic information concerning areas about to be invaded.

Army engineers have developed methods of interpreting the topography and of preparing topographic maps from the photographs, but they can not be expected to be able to read from the pictures the

[14] Y. Henderson, *Am. Jour. Physiol.*, 25: 395, 1910; 27: 152, 1910; Y. Henderson and S. C. Harvey, same journal, 46: 553, 1918; Y. Henderson and T. B. Barringer, Jr., same journal, 31: 289, 352.

[15] E. M. Landis, *Physiol. Rev.*, 14: 404, 1934; C. K. Drinker and J. M. Yoffey, "Lymphatics, Lymph and Lymphatic Tissue," p. 279. Harvard University Press, 1941.

[16] From βραδύς slow and ροία flow. With thanks to my classical colleague, Professor G. L. Hendrickson.

[17] Y. Henderson and H. W. Haggard, *Jour. Am. Med. Asn.*, 78: 697, 1922.

[18] Y. Henderson and H. W. Haggard, "Noxious Gases" (revised edition), Reinhold Publishing Company, 1942.

[19] Y. Henderson and H. W. Haggard, *Jour. Pharmacol.*, 11: 189, 1918.