therefore, they are not terminal, is based on the incorrect premise that terminal arteries cannot be thus injected, and has no weight against the positive evidence of the complete failure of nutrition following closure." As I interpret the process, the absence of anastomosis further suggests the existence of an additional source of energy; but the cardiac arrest after ligation of the coronary also indicates that compensation from the opposite heart can only be gradually established. On the whole, the coronaries of the right side are as important as if they alone supplied the needs of the functions of that side. The granules β and the adrenal secretion are furnished to compensate for the absence of *arterial* blood in the right auriculo-ventricular cavities and in their Thebesian channels; but, the right coronaries being the only source of one of the three *necessary* factors of the process, their obliteration means as much as that of the left coronaries does to the left heart.

We can also understand why the contractile elements of the primary fasciculi are bare. They are constantly bathed in the plasma from which they obtain the granules β that enter into the formation of their myosinogen. The absence of oxygen in this fluid renders it perfectly harmless to the delicate structures that surround the primary and secondary bundles of muscle-fiber, and to the net-works of arterial capillaries that hug the bare fibers. The latter, by a rapid absorption,—which the presence of sarcolemma would counteract,—are constantly forming their products of metabolism: *i.e.*, myosinogen. The arterial capillaries, "coated, on their external surface, with flat connective-tissue cells" (Berdal), when they cross the spaces of Henle, being the only carriers of oxygen, normally become the active factors of nutrition and function. Their blood is the normal excitant—as elsewhere. The venous blood brings the granules β; the adrenal secretions, by contracting the cardiac walls, forces it into the Thebesian channels; the bare muscle-fibers absorb the granules and convert them into their own particular kind of fuel, myosinogen; the capillary blood supplies the energy for this metabolism—oxygen—and simultaneously sustains, again with its oxygen, the combustion processes upon which the continuous work of the organ depends. Here, as elsewhere, the potential energy of

the chemical agencies present becomes converted into mechanical energy, which manifests itself as visible motion.

The left heart—the coronaries of which are larger than those of the right—presents anatomical features which modify, in a measure, the manner in which its physiological functions are performed. Both its auricle and ventricle containing arterial blood fresh from the heart, the Thebesian circulation does not appear to fulfill the primary rôle it does in the right heart. Indeed, the various experiments of Pratt and his predecessors and my own careful examination of the ox-heart distinctly show that the Thebesian circulation of the left heart, as regards intraventricular orifices, is much less important than that of the right heart. Still, the evident permeability of the interventricular septum and the histology of the left myocardium suggest that the left heart must receive material aid from the adrenal secretion and its granules β. This feature will again be referred to in the twelfth chapter.

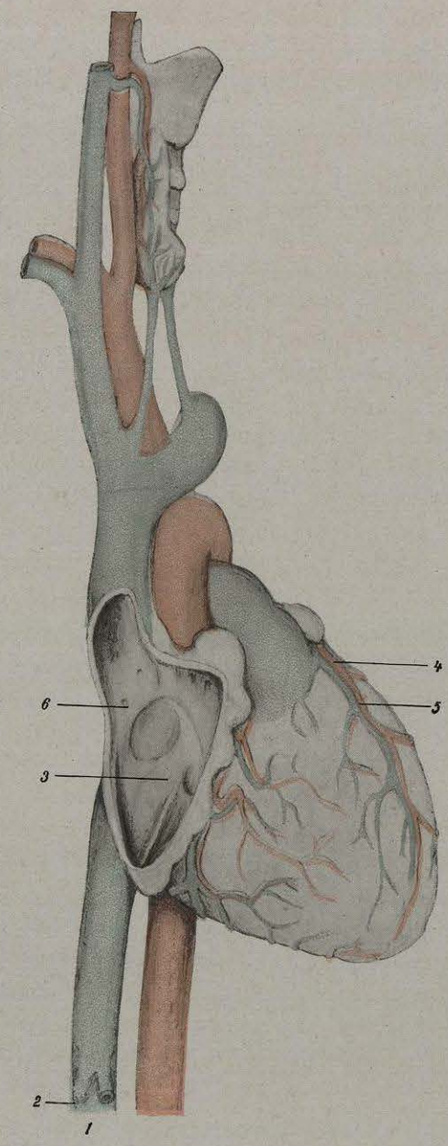
A feature that may be considered as demonstrated, and common to both sides, is the return of the blood, whether its source be the Thebesian or coronary systems, by way of the coronary veins. We have seen that Langer expressed the opinion "that the foramina Thebesii in the ventricles communicate with the veins by capillaries alone." My conception of the process involved would necessitate such an arrangement as regards the right heart. Indeed, so direct is this connection that even such viscid substances as starch and celloidin were found by Pratt, when introduced into the coronary veins of the ox, to emerge from the foramina Thebesii. Still, we could hardly expect such a free transit on the left side of the organ, inasmuch as the presence here of arterial blood only would suggest the presence of a structural organization similar to that of ordinary muscles. Indeed, referring to the vascular connections of the left heart, Pratt says: "So intimate a connection, however, between the coronary veins and the vessels entering the left ventricle I have not yet been able to demonstrate." Again, on the right side the connection with coronary veins must evidently be a physiological one, since "a small, but steady, stream of venous blood issued from them" when the veins were incised after the right ventricle had been filled with defibrinated blood.

But "no flow of blood occurred from the artery, although there was a free escape from an incision in an accompanying vein" in an experiment similar to that previously referred to, also performed by Dr. Pratt. In fact, it appears to me very doubtful whether even the capillary communication between coronary arteries and the Thebesian vessels, referred to by the latter observer in his conclusions, at all exists—at least in the walls of the right heart. Even disregarding my views, it seems evident that the admixture of venous blood with the arterial blood would greatly reduce and perhaps annul the functional efficacy of the latter as an oxidizing agent.

We can now understand how the adrenal secretion so greatly influences cardiac activity. An increase of it augments the force of the contraction, but the heart does not dilate as promptly nor perhaps as completely; hence its action is slower, but more forcible; we have seen that this represents the primary effect of all drugs sufficiently active to stimulate the adrenals. A still greater quantity of adrenal secretion increases the violence of cardiac action; the vessels are tense, and ecchymoses, hæmaturia, epistaxis, etc., may ensue. The heart acts normally, however, in the sense that its diastole is almost complete. Continuous cardiac stimulation through excessive production of adrenal secretion, due in turn to excessive production of iodothyrin, as in exophthalmic goiter, causes the heart to contract before it has exhausted its complete diastole and to work within a narrower field. Its contractions are sharp, but rapid: the type of the "cramped heart." Increase of adrenal activity involves increase of oxidizing substance; hence the left heart is correspondingly stimulated. When, however, adrenal insufficiency occurs, the phenomena follow an opposite course; when total inhibition of the adrenal system ensues, the vascular walls, losing all their functional stimuli,—the adrenal secretion, the granules β, and the oxidizing substance,—gradually cease their contractions and lapse into diastole.

THE INNERVATION OF THE HEART.

We are again brought, by analysis, to the realization that the efferent nerves distributed to the heart *incite* and *govern* functional activity but contribute nothing to the continuation



MECHANISM OF CARDIAC ACTION. *[Sajous.]*

1, Inferior Vena Cava, the blood of which contains Adrenal Secretion. 2, Hepatic Veins, the blood of which contains granules β derived from the Liver. 3, Right Auricle. 4, One of the Coronary Arteries. 5, One of the Coronary Veins. 6, One of the Foramina Thebesii.

of vital processes *per se*. Indeed, in the heart they do naught else than in other parts of the organism. One set of nerves distributed to the cardiac arteries provokes dilation to increase cardiac activity; another set causes constriction of these vessels when cardiac activity is to be reduced. "The rich nervous supply of the heart is derived from the coronary *plexuses*," says Piersol, "and *includes* numerous medullated fibers coming from the *pneumogastric* as well as the non-medullated *sympathetic* fibers proceeding from the cervical ganglia. Numerous microscopical ganglia are found along the course of the large nerve-trunks accompanying the branches of the coronary arteries, especially in the longitudinal interventricular and in the auriculo-ventricular furrows. Many additional small groups of ganglion-cells occur within the muscular tissue associated with the fibers supplying the intimate structure." Briefly, according to prevailing teachings the vagus and sympathetic are the nerves which govern the functions of the heart.

Is this true? In the light of my own views, it is subject to doubt; and, precisely as I have shown it to be the case with the kidneys, all the nerves supplied to the heart belong to the sympathetic system.

ACCELERATION.—Legallois, early last century (1812) urged that the nerves which increased the beats of the heart in a given time belonged to the sympathetic system. Although vigorously attacked by Bezold and others, this doctrine has steadily gained ground, and most investigators, including Heidenhain, Langley and Gaskell have accepted Legallois's view. It becomes a question, however,—in the light of my views,—whether acceleration represents the motor phase of cardiac action, and therefore, whether or not as in the kidney, the sympathetic fulfills the rôle of motor, *i.e.*, of vasodilator nerve. That it does is shown by the experiments of E. and M. Cyon[16] who found that occlusion of cardiac vessels did not cause acceleration—in other words that it was not by *reducing* the blood supplied to the heart walls that the accelerators acted upon the heart. On the other hand, as will be shown under the next heading, constriction of the cardiac arteries, *i.e.*, dimi-

[16] E. and M. Cyon: Archiv f. Physiol., 1867.

nution of the blood supplied to the cardiac muscle, slows the heart's action. Indeed, Baxt[17] observed a distinct antagonism between the vagi in the neck—owing as shown below to the presence of cardiac vasoconstrictor fibers in this nerve—and the accelerators, when stimulated simultaneously. The vagi suppressed the accelerators invariably, in fact, and irrespective of the strength of the current. It is evident, therefore, that acceleration is not due to constriction of the cardiac arteries, and that the sympathetic accelerators must act upon the heart by producing dilation of these vessels.

The vasodilator properties of the accelerators have, in fact, so legitimate a claim to recognition that in his recently published review of our knowledge on the subject Carvallo[18] remarks: "The first thoracic ganglion, or stellate ganglion seems to contain vasodilator fibers which almost always cause augmentation of speed." He forcibly illustrates this fact by a table demonstrating that the vessels so influenced show *an increased blood-flow in a given time,* when the accelerator nerves are stimulated, and closes his review with the following words: "We may conclude therefore that the heart possesses a complete vasomotor apparatus the vasoconstrictor fibers of which reach it essentially by way of the vagus, and the vasodilator nerves by the stellate ganglia [first thoracic] and the annuli of Vieussens."

Briefly, "acceleration" represents an exacerbation of activity of the heart, and just as we found such increased activity produced by vasodilation and the admission of an excess of blood, in other organs, so do we find it here.

INHIBITION.—In the light of foregoing statements, this phenomenon should assert itself as a result of excessive constriction of the cardiac arteries and diminution of the blood supplied to the cardiac muscle. That such is the case suggests itself from various directions.

The inhibitory effect of excessive constriction of the coronaries is beyond question. Chirac[19] found that the beats of a dog's heart were soon arrested when one of the coronaries was

[17] Baxt: Arb. a. d. phys. Anst., Leipzig, 1875.
[18] Carvallo: Richet's Dictionnaire de Physiol., p. 347,
[19] Chirac: "De Motu Cordis," p. 121, 1698.

tied. Erichsen[20] observed a similar result after tying these vessels. Leonard Hill[21] referring to the investigations of Cohnheim and Schulthess-Rechberg,[22] McWilliams,[23] Bettelheim,[24] and others, also states that "ligaturing one of the large branches only is frequently sufficient to cause arrest." Again, Sée, Bochefontaine and Roussy[25] observed that substances capable of plugging the coronaries—lycopodium spores, for instance—also caused cardiac arrest. Porter[26] plugged the left coronary artery in nineteen dogs and says that "the closure of the artery was always promptly followed by arrest." As the result of closure by ligation in sixty-seven dogs, he reached the deduction that "the frequency of arrest is in proportion to the size of the artery ligated." As cardio-inhibitory impulses transmitted through the vasoconstrictors of both vagal trunks probably influence *all* the cardiac arterioles simultaneously, the ease with which the heart's action can be arrested by exciting the bulbar center is easily accounted for. Finally Kolster,[27] Porter,[28] and others have shown experimentally that the part of the heart supplied by an infarcted coronary artery degenerates.

Yet, if the vasomotor impulses inhibit the heart by causing excessive constriction of the coronaries and their offshoots, the effects on the heart wall must coincide with those resulting from deprivation of blood. Such is undoubtedly the case: E. Weber[29] observed that during partial inhibition the cardiac contractions were weakened, while Schiff[30] found that the muscular elements of the entire organ responded less or not at all to stimuli. François-Franck, Fischel,[31] and others observed that the cardiac walls were softer than usual. Foster[32] states

[20] Erichsen: London Hospital Gazette, vol. ii, p. 561. 1842.
[21] Leonard Hill: Schäfer's "T. B. of Physiol.," vol. ii, p. 1, 1900.
[22] Cohnheim and Schulthess-Rechberg: Virchow's Archiv, Bd. lxxxv, H. 3, S. 503. 1881.
[23] McWilliam: Jour. of Physiol., vol. viii, p. 296, 1887.
[24] Bettelheim: Zeit. f. klin. Med., Bd. xx, S. 436, 1892.
[25] Sée, Bochefontaine and Roussy: C. R. de l'Acad. des sci., T. xcii, p. 86, 1881.
[26] Porter: Jour. of Exper. Med., vol. i, p. 46, 1896.
[27] Kolster: Skandinav. Archiv f. Physiol., Bd. iv, p. 1, 1893.
[28] Porter: Pflüger's Archiv, Bd. lv, Hft. 7 u. 8, S. 366, 1894.
[29] E. Weber: "Handwörterbuch d. Physiol., Bd. ii, S. 42, 1846.
[30] Schiff: Archiv f. Physiol. Heilk., 9ter Jahrgang, S. 22, 1850-51.
[31] Fischel: Archiv f. exp. Path. u. Pharm., Bd. xxxviii, Hft. 3 u. 4, S. 228, 1897.
[32] Foster: "T. B. of Physiol.," sixth American edition, Phila., 1895.

that when the interrupted current is used to stimulate the vagal trunk, the heart remains in diastole, motionless and flaccid. When, however, the current is weak, the beats are only slowed and weakened. Coats[33] ascertained manometrically that the contractions were markedly reduced in force. Gaskell[34] and Stefani[35] found that the ventricular tonicity was reduced. Muskens[36] also found that stimulation of the vagus lessened the force of the contraction in the frog.

Gaskell[37] characterizes as "most striking" the attending *depression of activity.* Still, there is no loss of inherent muscular irritability, since, according to Foster,[38] a pin prick in the heart during inhibition may cause the organ to resume its beats; the morbid phenomena are, therefore, the result of a deficient supply of the nutrient components of the blood. Porter[39] states that "but little is known as to the constituents of the blood which are essential to the life of the mammalian heart," and that "an abundant supply of oxygen is certainly highly important." The manner in which the deficiency of these blood constituents causes the inhibitory effects is suggested in the following lines of Langley's[40]: "The decrease of rigidity in the inhibited muscular tissue shows that inhibition is not caused by the development of a contractile force acting in a direction opposed to the normal one and overpowering it. We are then brought to the conclusion that certain nerve impulses —the inhibitory nerve impulses—are able to *lessen* or to *stop* the chemical change *in the tissue* which leads to contraction."

The rôle of the "inhibitory" fibers (now generally considered as vagal, because they form part of the nerve bundles which have been known as the vagi, or pneumogastric nerves) thus corresponds with that of the sympathetic vasoconstrictors we have found, elsewhere, to restore the arterioles to their normal caliber after these vessels had been dilated by a motor or secreto-motor nerve to incite an exacerbation of functional

[33] Coats: Bericht d. k. Sachs. Gesellsch. d. Wissensch., S. 360, 1869.
[34] Gaskell: Philosoph. Trans., p. 1019; 1882.
[35] Stefani: Archives italiennes de biologie, T. xxiii, p. 172, 1895.
[36] Muskens: Pflüger's Archiv, Bd. lxvi, Hft. 5 u. 6, S. 328, 1897.
[37] Gaskell: Schäfer's "T. B. of Physiol.," vol. ii, p. 169, 1900.
[38] Foster: "T. B. of Physiol.," sixth American edition, 1895.
[39] Porter: "Amer. T. B. of Physiol.," vol. i, second edition, p. 148, 1900.
[40] Langley: Schäfer's "T. B. of Physiol.," vol. ii, p. 616, 1900.

activity. Langley's observation gives precision to my view in this connection; interpreted from my standpoint, it is the diminution of blood in the cellular elements which serves "to lessen or to stop the chemical change in the tissue which leads to contraction." Can we logically, in view of the secreto-motor rôle ascribed by physiologists to the vagus in other organs, admit that in the heart its action is the opposite? That the so-called "inhibitory" nerve is composed of sympathetic fibers which carry on the same functions they do in other organs, is therefore evident.

Should we under these conditions consider the sympathetic as "inhibitory"? I have shown that inhibition is the result of excessive constriction of the arterioles. "Excessive" here obviously portrays a morbid or pathological condition, one of grave importance clinically. Indeed, as I will show in the second volume, many toxins and toxics are fatal owing to their vasoconstrictor influence on the cardiac vessels, and the morbid phenomena awakened are precisely those described above—those which the physiologist deems normal because they are expressions of a so-called physiological function he has termed "inhibition."

In my opinion the older term "moderator nerve" should replace the pernicious term now used, and "inhibition" be reserved for the expression of the morbid process which excessive constriction of the arterioles represents.

AUGMENTATION.—This action of the heart, *i.e.,* increase of its contractile power, must be due to an action other than that of acclerator nerves. Thus, von Bezold and Bever[41] and later Cyon[42] found that stimulation of the accelerator increased the number of beats of the heart, but not its power. This was confirmed by other investigators. Again the mode of action of the augmentor nerve differs strikingly from that of other cardiac nerves; Foster,[43] for instance, writes: "In contrast with the case of the vagus fibers, a somewhat strong stimulation is required to produce an effect; the time required for the maximum effect to be produced is also remarkably long." These

[41] Bezold and Bever: Untersuch. a. d. physiol. Lab. zu Wurzburg, Bd. ii, 1867.
[42] Cyon: *Loc. cit.*
[43] Foster: *Loc. cit.*, p. 203.

facts suggest that acceleration and augmentation are separate functions. Indeed, the delay in the augmentation of power, as compared with the acceleration, is explained when, as I urged a few years ago,[44] the adrenal secretion is regarded as the source of the increased cardiac power. This is sustained by many facts. Thus, while Noel Paton[45] refers to the "augmentors and accelerators" as small medullated, *i.e.*, sympathetic, fibers "which leave the spinal cord by the anterior roots of the second, third, and fourth dorsal nerves passing to the stellate ganglion," I have shown that the three above-mentioned roots are also precisely those through which the nerves which pass to the sympathetic chain and thence down to the splanchnic, to finally reach the adrenals. On stimulating these nerves, therefore, an experimenter not only excites the accelerators which pass to the heart via the annulus of Vieussens, but also the nerve-paths to the adrenals.

This accounts for the fact that while a large group of investigators including Cyon, Bezold, Schmiedeberg, Boehm and Bowditch observed acceleration without increase of power, others, equally competent, including Heidenhain, Mills, Roy and Adami, and Bayliss and Starling observed both phenomena. Indeed Schmiedeberg and Bowditch both urged the presence of two different sets of nerves to account for these specific effects, the one set influencing the cardiac beats, the other "acting upon the blood-pressure without influencing frequency." Now, the marked influence of the adrenal secretion upon the blood-pressure is well-known, and the delay in the appearance of "augmentation" is explained when it is borne in mind that the activity of secretory organs had to be awakened before the "augmentation" and the rise of blood-pressure could become manifest. Biedl,[46] in fact, found that stimulation of the divided splanchnic only caused an increased production of adrenal secretion after 7 to 9 seconds.

I submitted in the two preceding sections, the reasons which had led me to conclude that the adrenal secretion contributed to the contractile power of the right ventricle which

[44] Sajous: Jour. Amer. Med. Assoc., Feb. 4, 1905.
[45] Noel Paton: "Essential of Human Physiol.," p. 243, 1905.
[46] Biedl: *Loc. cit.*

it reaches with the venous blood of the inferior vena cava. Now, Brown-Séquard[47] had many years earlier (1853) urged the predominating influence of the blood of this vein upon cardiac dynamism, a view sustained by Radcliffe (1855); but Castell having found that a frog's heart when detached failed to beat with increased vigor in carbonic acid gas, and overlooking the fact that some other substance in the venous blood might have acted on the heart, physiologists disregarded Brown-Séquard's observation. Additional evidence to this effect is submitted in the second volume.

The presence of "augmentor" and "pressor" fibers in the sympathetic splanchnic accounts for the fact long ago recorded by von Bezold and Bensen,[48] that section of both splanchnics lowered the blood-pressure as much as section of the spinal cord in the cervical region, while Strehl and Weiss found that, after removing one adrenal, the blood-pressure could be lowered by clamping the suprarenal vein of the remaining organ, thus depriving the blood of any adrenal secretion, and that by releasing this vein the blood-pressure was soon restored to its previous level. As I view the process, however, excitation of the lower segment of the upper sympathetic cord after dividing it should raise the blood-pressure. Bezold found that this procedure raised the blood-pressure as much as *seven times* its initial level; Ludwig and Thiry showed, moreover, that the same result could be obtained after severing all the nerves to the heart.

Augmentor effects attended by a rise of the blood-pressure may also be produced through the intermediary of another organ. Cyon and Aladoff[49] found that stimulation of the annulus of Vieussens (which also contains pure accelerator fibers) raised the blood-pressure. Cyon had already found in 1867 that when the cervical sympathetic was divided on a level with the inferior cervical ganglion, and its *upper* segment was excited the strength of the heart-beats was markedly increased.

[47] Brown-Séquard: Exper. Researches applied to Phys. and Path., N. Y., London, and Paris, 1853.
[48] Von Bezold and Bensen: Neue Würzberger Zeitung, 1866; Verh. d. Phys. med. Gesells., Würzburg, January, 1867.
[49] Cyon and Aladoff: Bull. de l'Acad. des Sci. de St. Petersburg, vol. vii, 1871.