has been much discussion in physiology as to the nature of the action of the dilator fibers. The muscular coat of the small arteries runs transversely to the length of the vessel, and it is plain that when stimulated to greater contraction through the constrictor fibers it must cause a narrowing of the artery. It is not so evident how the nerve impulses carried by the dilator fibers bring about a widening of the artery. At one time peripheral sympathetic ganglia in the neighborhood of the arteries were used to aid in the explanation, but, since histological evidence of the existence of such ganglia is lacking, the view that seems to meet with most favor at present is as follows: *the dilator fibers end presumably* in the muscle of *the walls of the arteries,* and when stimulated their impulses *inhibit the tonic contraction of this musculature and thus indirectly bring about a relaxation.* Dilatation caused by a vasodilator nerve fiber always presupposes therefore a previous condition of tonic contraction in the walls of the artery, this tonic condition being produced either by the action of vasoconstrictor fibers, or possibly by the intrinsic properties of the muscle itself."

I conclude, therefore, that (1) *vasodilation is due, in the case of arteries and veins, to the diminution of blood-plasma and, therefore, of adrenoxidase, in the muscular layer of these vessels;* (2) *the blood-plasma being supplied to the vascular walls by the vasa vasorum, it is through contraction of these nutrient vessels that dilation of the vessels is caused;* (3) *the vasa vasorum receiving their blood-plasma from larger arterial vessels supplied with vasoconstrictor nerves, it is through vasoconstriction of these vessels that the volume of blood circulating through the vasa vasorum is diminished;* (4) *it is therefore by vasoconstrictor action that vasodilation is produced, "vasodilator nerves" having no existence in fact;* (5) *vasodilation being caused by constriction of the nutrient arteries of a vessel, the vasomotor nerves supplied to these nutrient vessels should not be termed "vasodilators" but "stricto-dilators."*

As Stewart[27] states, the fact that "an organ *in action* in general receives more blood than the same organ in repose" is "a physiological law of wide application." In the light of the evidence adduced, this constitutes the cardinal feature of all functional processes since it is to the presence of adrenoxidase in increased quantities that any exacerbation of activity, whether it be contraction or secretion, is due. It is apparent, therefore, that *this mechanism of vasodilation is that through which all exacerbations of activity in any organ, whether belonging to the alimentary, circulatory, locomotor, visual, auditory, or any other system, is incited and sustained.*

[27] Stewart: "Manual of Physiol.," fourth edition, p. 335, 1900.

The influence of this mechanism will become evident under the next heading.

THE POSTERIOR PITUITARY THE SEAT OF A CENTER (THE ADRENO-THYROID CENTER) THROUGH WHICH THE TEST-ORGAN INFLUENCES THE SECRETORY ACTIVITY OF THE ADRENALS AND THYROID APPARATUS.

Leonard Hill,[28] in a review of our knowledge upon the mechanism of the circulation, writes: "In the rabbit, from the junction of the vagus and superior laryngeal nerves, there arises by two roots a fine nerve, which courses down the neck. On excitation of the *central* end of this nerve, Ludwig and Cyon witnessed a surprising fall of arterial pressure, accompanied by a slight decrease in cardiac frequency. The peripheral end failed to give any response to stimulation. Thus the purely afferent nature of the nerve was established." . . . . . "This nerve was named, by Ludwig and Cyon [in 1866], the depressor, for it possessed the power of depressing the arterial tension by 30 to 50 per cent. Ludwig and Cyon observed that, on stimulating the depressor, the kidney flushed red with blood, while the fall of arterial tension became insignificant after section of the splanchnic nerves." . . . . . "In different mammals, many variations are to be marked in the course of this nerve, but fibers with a depressor function are to be found." . . . . . "In man the homologous nerve arises from the vagus from the junction of the vagus and superior laryngeal nerves, but quickly joins again the main trunk of the vagus." . . . . . "Almost all parts of the vascular system can be thrown into dilatation by the depressor nerve."

[28] Leonard Hill: Schäfer's "T. B. of Physiol.," vol. ii, p. 59, 1900.

The manner in which this effect is produced is still obscure: "The question is one not definitely settled," according to Hill, "and no conclusion as to the exact method of action of this nerve can be drawn." That it is not due to excitation of what he terms a "hypothetical vasodilator center" is suggested by the fact that vasodilator nerves "are easily exhausted by artificial stimulation," while the depressor is "inexhaustible." Cyon himself denies any relationship with such a center. As I have pointed out, moreover, the latter is not required to explain vasodilator phenomena. In fact, the spinal system cannot transmit the vasodilator impulses reflexly, since, as stated by Hill, after "dividing the spinal cord in the dorsal region, excitation of the depressor still causes a fall of arterial pressure." This obviously eliminates the vasomotor center also. Indeed, Porter and Beyer,[29] in an experimental study of this feature of the problem, state that they found "no evidence to warrant the opinion that the depressor nerves have special connections with the cells in the vasomotor center associated with the splanchnic fibers." Now, since as stated by Hill, "the splanchnic area is by far the most important seat of dilatation provoked by the depressor nerves," it is evident that the vasomotor center has nothing to do with the process. This leaves the latter totally unexplained.

This result is not surprising, in view of the fact that the functions of the pituitary body and of the thyroid gland, as I have interpreted them, alone make it possible to understand the process through which the depressor produces vasodilation. A comprehensive study of the question, which can only be represented here by a few salient facts, has led me to conclude that the depressor nerve produced this phenomenon by inhibiting the functions of the thyroid gland and pituitary body, and through the latter that of the adrenals.

Laulanié[30] states that the *pituitary body* "is in relation with the sympathetic, the vagus, and the depressor nerve"—a fact established by Cyon's experiments. That fibers of the cervical sympathetic are distributed to the pituitary body through the carotid plexus is well known. We have seen, moreover, that disorders of the anterior pituitary accompanied

[29] Porter and Beyer: Amer. Jour. of Physiol., vol. iii, p. 23, 1900.
[30] Laulanié: "Eléments de Physiologie," second edition, p. 488, 1905.

by local congestion give rise to glycosuria.[31] Now Cyon and Aladoff[32] found that lesions or removal of the upper thoracic or inferior cervical ganglia, or division of the loop of Vieussens, caused diabetes. All these contain sympathetic fibers which ascend to the superior cervical ganglion. Pavy[33] also states that "of all the operations on the sympathetic of the dog that have as yet been performed, removal of the superior cervical ganglion the most rapidly and strongly produces diabetes." As the fibers of the upper portion of the sympathetic other than those distributed to the pituitary supply various structures of the eye, those to the pituitary can alone explain this phenomenon. The manner in which this procedure causes diabetes is plain under these conditions: the sympathetic terminals to the pituitary being, as elsewhere, vasomotor, division of the nerve causes passive dilation of the vessels distributed to this organ, and the resulting congestion of the anterior lobe (by far the larger of the two, and the seat of the test-organ) gives rise to glycosuria by stimulating the adrenals. As previously stated, Blum, Croftan, Herter and others found that adrenal extract, adrenalin, etc., caused glycosuria.

Judging from the fact that vasodilation thus produced elsewhere in the body is temporary, however, the glycosuria should likewise be ephemeral: Pavy especially mentions the "temporary nature" of the marked diabetes following the experimental operation. On the other hand, if division of a nerve causes vasodilation, it is obvious that stimulation of the upper segment of that nerve should cause vasoconstriction. This is the rôle played by the depressor: forming part, as it does, of the cervical sympathetic, it was the nerve which, when cut by Pavy, caused vasodilation in the anterior pituitary and glycosuria, and which, conversely, causes vasoconstriction in this organ when its central or upper end is stimulated. The same effect is produced when the impulses (the nerve being, we have seen, entirely afferent) originate in the heart; the functional activity of the adrenal center being lowered by the contraction of its vessels, that of the adrenals is restrained in

[31] *Cf.* this vol., p. 1021.
[32] Cyon and Aladoff: Bull. de l'Acad. des sci. de St. Petersburg, vol. vii, 1871.
[33] Pavy: Proceedings Royal Soc. of London, vol. x, p. 27, 1859.

proportion and, less adrenal secretion being secreted into the blood, the vessels of the body at large dilate.

Under these conditions, division of the cervical sympathetic, by causing congestion of the anterior pituitary, and, therefore, stimulation of the adrenals, should antagonize (through the rise of vascular tension and blood-pressure caused by the secretion of the latter organs) the depressor action: Hill[34] states, referring to the lowered pressure caused by the vasodilation of depressor origin: "This fall is abolished by section of the cervical sympathetic nerves." Again, as the end-result is due to inhibition of the adrenals and diminution of their secretory activity, other means capable of interfering with their functions should also reduce the vascular tension and the blood-pressure—the results of vasodilation. Oliver and Schäfer have shown, as is well known, that adrenal extracts cause a marked rise of the blood-pressure. Strehl and Weiss,[35] on the other hand, found that clamping of the adrenal veins caused it to decline, and moreover, that on releasing the vessels the pressure would return to the normal.

The depressor nerve does not supply vasoconstrictor fibers to the pituitary body alone, however. Cyon[36] has recently studied the action of this nerve upon the vessels of the thyroid gland and found it very marked. He noticed, moreover, that it influenced correspondingly the abdominal and peripheral vessels. The nerves were found to be distributed to the arteries and were of two kinds, *vasoconstrictor* and *vasodilator*, and to reach them either by way of the superior laryngeals or through the plexus often formed by the depressor with the sympathetic and vagal nerves.

What are the functions of these vasoconstrictor and vasodilator nerves?

As to the *vasoconstrictor* branches, E. Cyon,[37] in a review of his experimental work upon the innervation of the thyroid, states that its "vasoconstrictors are sympathetic fibers." He found, moreover, that the depressor sent a branch to this organ, and that "the heart had a powerful regulator influence" on the quantity of blood circulating through it. On the other

[34] Hill. *Loc. cit.*, p. 162.
[35] Strehl and Weiss: Pflüger's Archiv, Bd. lxxxvi, S. 107, 1901.
[36] Cyon: Archiv f. d. gesam. Physiol., Bd. lxx, S. 126, 280, 1898.
[37] E. Cyon: Arch. de Physiol., T. x, p. 618, 1898.

hand, a clinician, Murray,[38] observed that "the effect of prolonged administration of thyroid upon the healthy gland is to cause a condition of pallor, some diminution in weight, slight diminution in size of the gland, but without any microscopic evidences of atrophic changes." Here we have precisely the condition produced by a similar process on the pituitary. When constricted the arteries allow less blood—and, therefore, fewer blood-cells—to enter the organ, and its functional activity is reduced. In other words, through the constrictor branches it sends to the pituitary body and to the thyroid, it reduces simultaneously the functions of both organs.

The fact that the depressor nerve causes vasoconstriction accounts for the heretofore paradoxical observation that, as stated by Hill, depressor effects cannot be obtained after the injection of strychnine—in toxic doses, I would add. These, by causing general vasoconstriction, affect in a similar way the thyroid and the pituitary body. The depressor producing likewise vasoconstriction, its effects are forestalled. Indeed, Oliver and Schäfer[39] found that depressor effects cannot be obtained "while the arteries are contracted by intravenous injection of suprarenal extract."

These various facts have served to bring out an important practical feature, concerning the avowed purpose of the depressor in the organism: Can we conclude with Cyon that, as he says, this nerve enables the heart "to control the resistance which opposes its evacuation," or, in other words, to provoke vasodilation, when excessive general vasoconstriction causes the blood-column to resist unduly the heart's contractions? If such were the case, why does not stimulation of the central end of this nerve overcome the general vasoconstriction produced by strychnine and adrenal extract? It is evident that this cannot be the main function of the depressor, for, as is well known, the vascular pressure is raised dangerously by various poisons, especially during spasm, and there is no evidence that the depressor fulfills the rôle ascribed to it by Cyon. Its true rôle is of another kind.

This introduces the function of the *vasodilator* fibers which the depressor supplies to the thyroid.

[38] Murray: Lancet, Mar. 18, 1899.
[39] Oliver and Schäfer: Jour. of Physiol., vol. xviii, p. 230, 1895.

In the light of the conclusions submitted under the preceding heading, the vasodilation observed by Claude Bernard in the maxillary gland indicates increased functional activity, and that this applies to all other organs. As I have shown, moreover, that leucocytes virtually carry on the functions of the thyroid, this vasodilation involves the presence of a larger number of leucocytes in this gland, and therefore, hyperactivity of the organ. As this is manifested by increased secretory activity, an excess of thyroidase should be produced. Now various clinicians, Roger and Garnier,[40] Odoacre Torri,[41] Vincent[42] and others, have observed that in various diseases, including the infections, the thyroid was not only *overactive*, but that it *produced an excess of colloid*, its secretion. In view of the facts (1) that the posterior pituitary incites functional activity in organs belonging to the field of the vagus; (2) that toxic wastes, certain toxins and poisons stimulate the test-organ; and (3) that the depressor nerve also sends fibers to the pituitary body, as shown by Cyon, the manner in which this is brought about suggests itself, viz.: the pathogenic elements of the diseases referred to, which include exanthemata, tuberculosis, typhoid fever, etc., stimulated the adrenal center as usual, and, therefore, the adrenals; but, *in addition* to this, and through the depressor vasodilator fibers to the thyroid, the secretory activity of this organ.

This affords a complete mechanism for automatic defence: The excess of thyroidase to sensitize and soften (as agglutinin) the bacteria and other pathogenic elements, and thus prepare them for destruction; the excess of adrenoxidase to increase the functional activity of the pancreas and leucocytogenic organs, and to charge the blood with trypsin, nucleoproteid granules, and aggressive phagocytes. All these substances, adrenoxidase, trypsin, nucleo-proteid and phagocytes, then unite to destroy the pathogenic agent, previously prepared by the thyroidase to insure its dissolution.

A cardinal feature of the whole defensive mechanism asserts itself in this connection: The vasodilator fibers of the

[40] Roger and Garnier: Presse méd., vol. vi, p. 181, 1899.
[41] Odoacre Torri: Policlinico, vol. vii, pp. 145, 226, 280, 1900.
[42] Vincent: Bull. et mém. de la Soc. méd. de hôpitaux de Paris, 3e. série, 23annee, p. 598, 1906.

thyroid (some of which also supply the parathyroids) jointly constitute the *thyro-parathyroid secretory nerve,* just as the vasodilator nerves supplied to the adrenals constitute the *adrenal secretory nerve.* Inasmuch as both the thyro-parathyroid and adrenal secretions form part of the blood's bacteriolytic and antitoxic substance, it is evident that both must, in order to insure the full efficiency of the latter, be secreted simultaneously in appropriate proportions. It follows that this function must be governed by a single center, the *adreno-thyroid center.*

Again, inasmuch as it is through the test-organ that all agents which increase the functional activity of the adrenals and through them the defensive properties of the blood and its cells, enhance oxygenation and function throughout the entire organism, it follows that it must also be through this organ that the functional activity of the thyroid and parathyroids is increased. Whereas, however, the test-organ is a sensitive structure, precisely as the olfactory area of the nasal cavities is a sensitive structure (of which, in fact, it is, as we have seen, the homologue), its impulses are sensory and afferent, and as such, therefore, incapable of inciting or augmenting function directly, it is evident that, as is the case throughout the entire nervous system, they must first of all be converted into motor stimuli. In view of the evidence, histological, clinical, physiological and anatomical, submitted, the posterior or neural lobe of the pituitary not only receives fibers from the test-organ, but it also projects nerve-chains to the base of the brain, which ultimately end in the adrenals and in the thyroid apparatus. It is in the posterior lobe of the pituitary, therefore, that the adreno-thyroid center is located, and when drugs, poisons, catabolic wastes, etc., awaken a protective reaction of the test-organ, it is through this center that the secretory activity of the adrenals and thyroid g'and and glandules is activated.

On the whole, all the evidence submitted in the foregoing pages, supplemented by that embodied in the preceding chapters, tends to show: (1) *that the test-organ governs the secretory activity of the adrenals and of the thyroid and parathyroids through the intermediary of a center located in the posterior pituitary body, the adreno-thyroid center;* (2) *that when drugs, poisons, toxins, waste-products, etc., provoke a defensive*

reaction of the test-organ, it is by exciting simultaneously the adrenals and the thyroid apparatus, through the adreno-thyroid center, that it (the test-organ) increases the proportion of adrenoxidase and thyroidase in the blood; (3) *as adrenoxidase, by hastening metabolism, provokes leucocytosis (including an increase of phagocytes) and an increase of nucleo-proteid and trypsin, and combines with these bodies to form the bacteriolytic and antitoxic constituents of the blood and of its phagocytes, while* (4) *thyroidase sensitizes (as opsonin) the pathogenic germs and substances to render them vulnerable to these defensive constitutents,* it follows: (5) *that the adreno-thyroid center, under the dependence of the test-organ, is the center through which all the body's auto-immunizing functions are governed.**

Hereafter, to avoid confusion, however, I will refer to this center as the "adrenal center" in most instances since the only clearly defined phenomena are those directly ascribable to bodies formed through the agency of the adrenals. It will be understood, thereby, that the "adreno-thyroid" center is meant and that the thyroid apparatus is always stimulated simultaneously.

The participation of the depressor nerve in this mechanism is shown conclusively from another direction:—Cyon[43] observed another important fact, viz., that when he injected iodothyrin—a thyroid extractive—the excitability of the depressor became intense and the vascular pressure declined often to two-thirds of the normal. In one instance, in fact, the animal died suddenly. Cyon ascribes death in such instances to paralysis of the vasoconstrictors. From my viewpoint, it is due to quite another and opposite cause—that previously referred to as of exceeding practical importance: excessive constriction of the vessels of the pituitary and thyroid, and, as a result, arrest of the vital functions owing to deficient supply of adrenoxidase and thyroidase. The general vasodilation produced is but a secondary or epiphenomenon under these conditions. As to the process through which iodothyrin evokes these phenomena, Cyon ascribes it to the fact that it increases

*Investigators refer to the thyroid gland as an organ capable of "governing" certain functions or morbid processes. The above facts show that the thyroid governs nothing; it is only a secreting gland, governed as are all other glands, by a nerve-center—the adreno-thyroid center, from my viewpoint—to which its fluctuations of activity and some of its diseases—exophthalmic goiter, for example—should be ascribed.

[43] Cyon: *Loc. cit.*

the *excitability* of the nerve. This harmonizes perfectly with my own view, since, as I have pointed out, the function of thyroidase is to *sensitize* all cells, to endow them, in other words, with *irritability.* Thyroidase *sensitizes* the nerve directly, therefore, by circulating with adrenoxidase, its ubiquitous companion, in the neurons composing it.

In accord with the evidence submitted, the vasoconstrictor effects produced by various drugs, even when administered in toxic doses (as will be shown farther on), are in no case counteracted by the depressor nerve; it is evident, therefore, that (1) *it is not the function of the depressor nerve, as now believed, to cause general vasodilation when excessive general vasoconstriction causes the blood column to offer undue resistance to the heart's contractions;* (2) *in practice the vasodilation witnessed when the central end of this nerve is stimulated experimentally, occurs only when excessive doses of thyroid extract are administered, because it adds to the blood what thyroidase it contains;* (3) *the excitability of the depressor nerve being increased artificially by this excess of thyroidase, it inhibits the functions of the pituitary and thyroid and by thus reducing the proportion of adrenoxidase (and thyroidase) in the blood reduces the vascular tension sufficiently, when toxic doses of thyroid extract are administered, to cause death.*

I must lay stress on the fact that this does not mean that the depressor nerve cannot produce vasodilation: It means only that general vasoconstriction, however marked, cannot itself provoke general vasodilation through the intermediary of this nerve. Inasmuch as it can inhibit the functions of the thyroid gland and anterior pituitary by constricting their arteries, it is able to reduce general oxygenation and metabolism throughout the entire body, including the muscularis of all vessels, thus causing them to relax, *i.e.,* to dilate. As I will show in the twentieth chapter, sleep is produced through the depressor nerve by a corresponding mechanism. Hence the fact that when stimulated experimentally, this nerve produces vasodilation. In other words, *the nerves which have been known as the "depressor nerves" are those through which the adreno-thyroid center regulates the circulation of the anterior pituitary body and of the thyroid apparatus.*

DRUGS WHICH ENHANCE THE DEFENSIVE PROPERTIES OF THE BLOOD BY PROMOTING THE FORMATION OF AUTO-ANTITOXIN.

In his review of the subject of Active Immunity, Lazarus-Barlow,[44] after referring to Pasteur's, Haffkin's and Wright's application of the principle of inoculation in various diseases, writes as follows: "Immunity may be conferred by repeated inoculation with small doses of virulent microörganisms. In this method it is obvious that a direct attempt is made to copy nature. The dose inoculated must, of course, be less than the minimal lethal dose. When the animal has recovered, it is found to possess a certain degree of immunity, and one is able, by gradually raising the dose of virus injected in successive inoculations of the same animal, to raise the degree of immunity which it possesses. Ultimately the animal may withstand with ease a dose equal to many times the dose which would at first have been fatal.

"The most important method we possess for obtaining acquired immunity is that introduced by Salmon and Smith in America. These investigators found that, if the sterilized products of the bacillus of hog-cholera be injected into pigeons, the birds became resistant to subsequent inoculations with the bacillus itself. This method is of vast importance, both from a practical and from a theoretical point of view. . . . . Numerous examples of immunity acquired in this manner are known, but the most striking are perhaps those obtained in the cases of *B. tetani, B. diphtheriæ,* and *B. pyocyaneus.*

"Just as, when conferring immunity by doses of virulent microörganisms, it is necessary to commence with doses far below the lethal dose, and to gradually increase the amount inoculated, so in this method of 'immunization by chemical products' it is necessary to begin with very small doses of the toxin and to gradually increase the dose as immunity is being acquired. If this process be carried out with care, an animal may in time acquire so great a degree of immunity that it will withstand an injection of many hundred times the dose of poison that would have, at first, killed it with certainty. This

[44] Lazarus-Barlow: "Manual of Gen. and Exp. Pathol.," p. 343, 1904.

method is adopted (in some cases in conjunction with inoculation of cultures of living and virulent bacilli) in the preparation of antidiphtheritic serum from horses. There is a limit, apparently, for each animal, beyond which an acquired immunity of this kind cannot be pushed.

"It has been found that an immunity may be acquired after feeding an animal with toxin. Little is known with reference to this method, but it is of great interest in connection with the beneficial results obtained in myxœdema by feeding with thyroids of the sheep."

It is my purpose to show in the following pages that, interpreted in the light of my views, several of our remedies, particularly *some* of those now characterized as "alteratives," behave as do toxins when introduced into the organism, in the sense that they confer upon the patient the power to resist infection. This, from my standpoint, is due, as previously shown, to a compound (adrenoxidase, nucleo-proteid and a zymogen), which, whether as trypsin, steapsin, amylopsin, etc. (according to the zymogen it contains) submits proteids, fats, glycogen, starches, etc., *and bacteria and their toxins as well,* to a process of digestion—a process which, according to the present teachings of physiological chemists, is one of hydrolytic cleavage.

Again, referring to "passive immunity," Lazarus-Barlow writes: "It was found by many observers, among whom Behring stands preëminent, that when an animal has, by any of the methods described above, been immunized against a given infective agent, the blood-serum of that animal, if inoculated into other animals, can confer upon them also an immunity against the same infective agent." The truth of this law he regards as "now firmly established. It has been demonstrated," he adds, "in the cases of rabies, of tetanus, of diphtheria, of pneumonia, and of other diseases. Ehrlich extended the range over which this law holds good by showing that animals may be actively immunized against ricin (the active principle of castor-oil beans) and abrin (the active principle of jequirity seeds), and that the blood-serum of such immune animals is able to confer passive immunity against ricin and abrin respectively in other animals. And Calmette,

whose work has been confirmed by Fraser, has shown that the same holds good with reference to animals immunized by successive doses against snake-venom." This refers, of course, to the various antitoxins, of which diphtheria antitoxin is the best known.

In the first volume I assimilated these antitoxins to the bacteriolytic and antitoxic constituents of the blood, whose origin I have traced in the foregoing chapters to the adrenals, the pancreas, the leucocytes and the thyroid apparatus. I have no ground to modify my opinion as shown in the last section of the present chapter. When, therefore, the serum of an immunized animal is injected into another animal, what *is* (from my standpoint) injected is merely a certain quantity of the bacteriolytic and antitoxic triad which had been caused to accumulate in the first animal's blood by inoculations. In other words, *diphtheria antitoxin and other antitoxins are antitoxic triads, derived from the adrenals, pancreas, leucocytes and thyroid apparatus,* and which when injected into the blood during infectious diseases, increase its bacteriolytic and antitoxic properties according to the quantity injected.

Interpreted in this manner, the first principle, that of introducing toxins into the blood to evoke immunizing principles, is the foundation of the entire defensive process—the militant weapon of which is the antitoxin. Now, this is precisely what, in the light of my views, some of our familiar remedies are able to do. In other words, *certain alteratives can cause the blood to become bacteriolytic and antitoxic by provoking the formation and accumulation therein of more or less antitoxin.*

To distinguish this antitoxin—produced by the organism itself under the influence of certain toxins and drugs—from antitoxins introduced into the body from without, I will refer to it hereafter as *auto-antitoxin.*

The examples submitted in this chapter of agents capable of provoking the formation of this substance are thyroid extract, mercury, iodine and its salts, and adrenal extractives. If all acted similarly, one would suffice as an example of at least a group, but (and it must be admitted that we are far

from such a fund of knowledge concerning the effects of individual toxins) each drug shows specific properties especially in the toxic phenomena they produce, which, as I will show, can be accounted for. In *thyroid gland,* for instance, we have an example of a drug capable of raising the blood's asset in auto-antitoxin, since it enhances markedly general metabolism. At a given time, however, the arteries begin to dilate and keep on doing so. The reason for this is plain: thyroidase acting directly, as shown by Cyon, on the depressor nerve, it causes general vasodilation by constricting the arterioles of the pituitary body, reducing thereby general metabolism in the vascular walls. *Mercury* presents another phase. Though likewise able powerfully to raise the activity of metabolism and the blood's supply in auto-antitoxin, it fails to provoke the formation of sufficient thyroidase to cause the depressor to control the pituitary body—the proportion of thyroidase added to the blood even by toxins being always very small. So marked is the stimulating action on the test-organ and adrenal center, that metabolism is increased to unsafe limits and excessive salivation, tissue destruction occurs, simply because the auto-defensive process has been converted into an auto-destructive process by an excessive quantity of auto-antitoxin in the blood. Not only are bacteria, toxins, etc., destroyed, but the blood-cells, and sometimes the tissue likewise. In *iodine* (and its salts), we have another powerful stimulant of the adrenal system, and the fact that it is the main constituent of the thyro-parathyroid secretion and that it keeps the blood well supplied with opsonins accounts for the value of this drug, since bacteria and the pathogenic elements are prepared for the digestive process to which the auto-antitoxin in the blood and phagocytes submits them. Finally, we have in the *adrenal extractives,* agents which increase directly metabolism in all tissues, and thus provoke the formation of more or less auto-antitoxin. But here we lack the fundamental attribute of the whole process, *i.e.,* they do not stimulate the test-organ directly. Hence their fleeting action, though they are very useful when the blood's most important function, oxygenation, must be promptly and energetically augmented, and when the morbid effects of hypocatabolism must be offset.