of the adrenal secretion is afforded by the fact that it accounts, as will be shown by a few examples, for the properties of the adrenal secretion and preparations that the prevailing restricted view fails to explain.

Increased oxidation clearly accounts, for instance, for the observations of Reichert, Morel, Lépine and others, referred to above, that even non-toxic doses of adrenal extractives produce a *rise* of temperature, or those of Israel[79] which showed the great frequency of fever in tumors of the adrenals, or those of Courmont[80] in which adrenal grafts produced without the least evidence of infection what he characterized as a "formidable hyperthermia." In the latter cases it persisted until death occurred. Nor is it an ephemeral phenomenon, as is the case with the rise of blood-pressure, in the experimental use of adrenal preparations, for, as Reichert observed in his experiments, the high temperature persisted as much as two hours in some of the animals.

Again, adrenal preparations are familiarly known to raise the blood-pressure; but, obviously this tells us only *what* they do, but not *how* they do it. This becomes clear, however, when the adrenal secretion as the active constituent of hæmoglobin is regarded as the oxidizing agent of the tissues, and, as such, an active factor in metabolism. The muscular elements of the arteries being themselves the seat of increased metabolic activity, they are caused to contract, thus raising the blood-pressure. As shown by Oliver and Schäfer, however, there is also a direct action on the arterioles, and by Meltzer[81] a similar action on the endothelium of the capillaries. This local effect is due also to the enhanced metabolic activity of the adrenal product, its identity as catalyzer enabling it to activate oxidation in any tissue with which it comes into contact.

The excessive growth of children caused by hypernephroma also finds its normal explanation in the inordinate oxidation, due to the overproduction of adrenal secretion. F. de Mira[81a] found experimentally that the adrenals stimulated growth in general. The surplus of metabolic activity clearly accounts for the enhanced nutrition.

[79] Israel, cited by Moffitt: Boston Med. and Surg., Jour., Oct. 8, 1908.
[80] Courmont: Congrès de Médecine Interne, Montpellier, 1898.
[81] Meltzer: Amer. Jour. Med. Sci., Jan., 1905.
[81a] F. de Mira: C.-r. de la Société de Biologie, Oct. 25, 1912.

In its relations to general diseases, the identity of the adrenals as the controlling agents of oxidation accounts for that ubiquitous symptom, *fever*, the mechanism of which has also remained obscure. This gives these organs a prominent place in pathology. Indeed, if the modern doctrine that fever up to a certain limit is the outward expression of an auto-protective or immunizing process is sound—and the bulk of evidence strongly sustains this view—the adrenals, as direct factors in fever, become also direct factors in protecting the body against disease. Their rôle in the economy thus assumes noble proportions in the extreme, since by their influence on tissue oxidation *the adrenals* sustain life, while through their participation in immunity they defend life.

Addison's disease may be due, as is well known, to tuberculosis, cancer, cirrhosis, and other organic disorders of the adrenals, or to pathologic changes in the solar plexus and semilunar ganglia. But *how* do these lesions cause the Addisonian syndrome in all its complexity? Many theories have been vouchsafed, but, in truth, as Anders[82] puts it, "the pathologic connection between the symptomatic phenomena of Addison's disease and the anatomic lesions has not been made out." Now, consider the disease with the adrenals as governing oxidation and metabolism: The adrenals being the seat of destructive lesions, these three conjoined functions increasingly show signs of deterioration; hence the low temperature and clamminess due to deficient oxidation; the marked and progressive asthenia, with great lassitude, due to inadequate metabolism in all muscles; the small and feeble pulse and weak heart action and steady lowering of the blood-pressure due also to inadequate metabolism in the cardiac and vascular muscles; the tendency to vertigo and the mental torpor due to ischæmia of the cerebrum, the result, in turn, of the general vasodilation and of the resulting withdrawal of blood into the deep vessels, and, finally, the bronzing, due likewise to vaso-relaxation and circulatory torpor, the latter entailing the deposition in the epidermis of what has been found chemically to be the oxidized adrenal product, *i.e.*, melanin.

The experimental production of glycosuria by injections of adrenalin reported by Blum, Croftan, Herter, and others is now

[82] Anders: "Practice of Medicine," p. 489, 9th ed., 1909.

familiar to every one. The labors of Pollak[83] have shown that, as I had previously suggested, this form of glycosuria was due to some relationship between the adrenal product and the hepatic glycogen. But what is this relationship? Here, again, the rôle of the adrenals in oxidation and metabolism supplies the explanation: By raising the blood's asset in oxygen, the adrenal active principle injected raises the rate of metabolic activity throughout the entire organism, including, of course, the pancreas. This organ being caused to secrete an excess of amylopsin, which in turn converts an excess of glycogen into sugar, the proportion of the latter in the blood soon exceeds the needs of the body, and the surplus is eliminated in the urine. The participation of the adrenals themselves in the process is controlled by various facts. Herter, for example, found that glycosuria was caused when the adrenals were compressed in such a way as to increase the outflow of secretion, while, conversely, ligation of the adrenal veins which transfer the secretion to the inferior vena cava caused the sugar to diminish rapidly, both in the blood and in the urine. That our resources in the treatment of diabetes are enhanced by due consideration of the part played by the adrenals in one of its forms is soon shown by therapeutic results obtained.

Many other disorders the pathogenesis of which is obscured and the treatment of which is unsatisfactory, mainly owing to the fact that the adrenals are overlooked in their pathogenesis, are described in detail in the second volume. The facts submitted in the foregoing pages will suffice, however, to suggest that *the function now attributed to the adrenals,* i.e., *that of sustaining the tone of the vascular system, is but an epiphenomenon of its true function: that of sustaining pulmonary and tissue respiration.*

THE GOVERNING CENTER OF THE ADRENALS.

THE PITUITARO-ADRENAL NERVE.

That organs fulfilling such important duties in the organism as the above should be governed by some nerve-center almost imposes itself when we consider that many functions of relatively minor importance—color vision, coughing, sweating, ear

[83] Pollak: Arch. f. exper. Path. u. Pharm., Bd. lxi, S. 149.

movements, etc.—are supplied with one. My researches in this connection first showed that:—

The governing center of the adrenals is neither located in the cerebrum nor in the medulla oblongata, but in some organ at the base of the brain.

Removal of both hemispheres does not influence temperature, as shown by Frédéricq,[84] Goltz, and others. Corin and van Beneden[85] found in fact that, in decerebrated pigeons, the oxygen intake and the carbonic acid output did not differ from that of normal pigeons. Pembrey[86] states moreover that "the rapid rise in temperature which occurs when a hibernating marmot awakens is not prevented by removal of the cerebral hemispheres." This applies as well to so high a mammal as the dog, in which, as shown by Goltz,[87] removal of the hemispheres, including a part of the optic thalami and corpora striata (whose functions are also annulled by removal of the cortex, the impulses of which they transform and transmit), did not interfere with any purely vegetative function. Evidently, therefore, although the hemispheres and the basal ganglia can, when the seat of lesions, cause a rise of temperature, the heat center is not located in these organs.

The base of the brain, however, asserts itself as a pathway for thermogenic impulses. While Tschetschichin, in 1866, Schreiber,[88] and Reichert[89] located a thermoaugmentor center in the pontobulbar region, Ott,[90] Tangl,[91] and Sakowitsch[92] obtained a marked rise of temperature by producing lesions higher up, *i.e.,* in the floor of the third ventricle and the tuber cinereum. But, as Richet has long held, and as Schäfer[93] states, examination of such experiments shows that "the results are closely dependent upon the establishment of an irritative lesion in parts which are either directly in or in close proximity to the path taken by motor impulses." On the whole, the thermogenic lesions in the basal tissues must have irritated nerve-paths from some structure beneath the hemispheres.

[84] Frédéricq: Arch. de biol., iii, p. 747, 1882.
[85] Corin and van Beneden: *Ibid.,* vii, p. 265, 1889.
[86] Pembrey: Schäfer's "Text-book of Physiology," i, p. 864, 1898.
[87] Goltz: Arch. f. d. ges. Physiol., li, p. 570, 1892.
[88] Schreiber: *Ibid.,* viii, p. 576.
[89] Reichert: Jour. Amer. Med. Assoc., January 18, 1902.
[90] Ott: Therap. Gaz., June 15, 1903.
[91] Tangl, cited by Ott: *Ibid.*
[92] Sakowitsch: Neurol. Centralbl., xvi, p. 520, 1897.
[93] Schäfer: *Loc. cit.,* ii, p. 717.

Further study of the question then showed that:—

The pituitary body sends nerve-fibers upward to the tuber cinereum and the walls of the third ventricle, and thence to the pontobulbar region and spinal cord.

As just shown, the heat center can only be located beneath the brain and basal ganglia. Now, anterior to the optic thalami, the corpora striata, and the seat of the thermogenic lesions produced by Ott and others, there exists no organ capable of generating nerve impulses by way of the tuber cinereum other than the pituitary body. The labors of many investigators in recent years have overthrown the view that any part of the pituitary body of man is vestigial. As Herring[94] concluded recently on histological grounds, "it is an organ of physiological importance." The various kinds of nerve-cells, neuroglia-cells, and ependyma-cells described by Berkley in the posterior lobe are of as great physiological importance, from my viewpoint, as any in the body at large. Cushing[95] recently confirmed by a large number of experiments the fact previously emphasized by many investigators, that complete removal of the pituitary invariably produced death.

Sappey, Luschka, Müller, and others of the older anatomists refer to the presence of nerve-fibers passing from the pituitary body along its pedicle, up to the third ventricle. But it was only after the Golgi method had been introduced that this fact could be placed on a solid basis. Ramon y Cajal[96] then found that the fibers passed upward to a large nucleus behind the optic thalami. Joris[97] also found histologically that "numerous fibers descend in parallel lines along the pedicle of the pituitary. They do not all come from the retro-optic nucleus," he writes; "some come from regions *posterior* to the infundibulum". . . Bearing directly upon the production of thermogenic impulses is the discovery by Gentès[98] of fibers which pass from the pituitary to the tuber cinereum. Andriezen[99] had also traced, in the white mouse, fibers from the pituitary to the pons.

We thus have a direct nerve path from the pituitary to the

[94] Herring: Quarterly Jour. of Exp. Physiol., i, No. 2, 1908.
[95] Cushing: Jour. Amer. Med. Assoc., p. 249, 1909.
[96] Ramon y Cajal: Anales de la Soc. española de hist. nat., 2a Seria, xxiii, p. 214, 1894.
[97] Joris: Mém. Couron. de l'Acad. Roy de Belgique, xix, part 10, 1908.
[98] Gentès: C. r. de la Soc. de biol., lv, p. 1560, 1903.
[99] Andriezen: British Medical Journal, January 13, 1894.

pontobulbar region—the identical tract along which, at various points, the lesions produced by Ott, Tangl, Sakowitsch, and Reichert provoked a marked rise of temperature. We will see presently that this path is continued down the cord, and that it eventually reaches the adrenals.

The next feature determined was a striking functional correlation between the pituitary and the adrenals. Schäfer and Herring[100] recently emphasized this parallelism not only as to their function, but also as to their development and structure. I ascertained, for example, that

The pituitary, like the adrenals, influenced general oxidation and the temperature, and also general metabolism and nutrition.

Although removal of the hemispheres does not influence the temperature, as we have seen, removal of the pituitary deeply affects this process. Marinesco[101] and Vassale and Sacchi[102] observed that it was followed by increasing hypothermia. This cannot be ascribed to operative shock, for Masay[103] first trephined the sella turcica to expose the pituitary, and allowed the animal to recover after this—the most violent step of the experiment. The result of subsequent removal was the same. Andriezen[104] and other authors also refer to a steady decline of temperature. Paulesco[105] noted that this decline was progressive until death occurred. Pirrone[106] states that the main symptoms are referable to the "vascular and respiratory systems and the temperature." The relationship with the respiratory process is further shown by the marked disturbances of this class, dyspnœa, polypnœa, etc., noted by Cyon, Andriezen, Masay, and other experimenters.

The impairment of general metabolism through deficient oxygenation must necessarily inhibit nutrition. Practically all investigators refer to rapid emaciation and cachexia as prominent symptoms. In a dog which survived sixteen days' removal of the organ, Thaon[107] observed "a progressive emaciation, followed

[100] Schäfer and Herring: Philos. Transactions, cxcix, p. 29, 1906.
[101] Marinesco: Bull de la Soc. de biol., p. 509, June 4, 1892.
[102] Vassale and Sacchi: Arch. ital. de biol., xxii, p. 123, 1895.
[103] Masay: Arch. de la Soc. roy. de sci. méd. et nat. de Bruxelles, xii, part 3, p. 1, 1903.
[104] Andriezen: *Loc. cit.*
[105] Paulesco: Jour. de physiol. et de path. gén., No. 3, p. 441, 1907.
[106] Pirrone: Riforma medica, February 25, 1903.
[107] Thaon: L'Hypophyse, p. 90, 1907.

by death in extreme cachexia." Caselli,[108] Pirrone,[109] and Masay[110] also allude to this phenomenon. Fuchs[111] and many other authors urge the close—though obscure—relationship between the pituitary and bodily metabolism. Striking evidence of the influence of the pituitary on metabolism and nutrition is afforded by its rôle in gigantism and acromegaly, the excessive growth during the period of hyperplasia of the organ, and the steady decline from the time degeneration of its anterior lobe begins. A relationship with the adrenals is suggested, moreover, by a familiar symptom of the cachectic stage of acromegaly, of which Harlow Brooks[112] says: "A general brownish pigmentation is present in the average case, which at times strongly resembles that found in Addison's disease."

Another feature attesting to the parallelism between the pituitary and the adrenals is that

The pituitary, like the adrenals, influences the blood-pressure.

Cyon[113] and subsequently Masay[114] found that excitation of the exposed pituitary caused a marked rise of blood-pressure—from 81 to 200 mm. Hg. in one instance. Masay attributed this action to the presence in the organ of a secretion which the excitation and accompanying pressure forced into the circulation. While no one can assert today that such a secretion is not produced by the pituitary body, the actual existence of such a secretion or its functions has not so far been demonstrated. The substance considered as such is rich in albuminous hæmoglobin, and it is the adrenal principle it contains which, in my opinion, causes the rise of blood-pressure obtained by injections of the extract. When the pressure is marked, the kidneys, being passively congested, dilate, and diuresis is caused. The effects observed experimentally are thus accounted for without the need of a secretion to do so. This applies also, from my viewpoint, to several so-called "internal secretions." Testicular juice or orchitic extract, for instance, is an oxidizing ferment and cata-

[108] Caselli: Studi anat. e sperim. sulla fisio-pat. della glandula pituitaria, 1900.
[109] Pirrone: *Loc. cit.*
[110] Masay: *Loc. cit.*
[111] Fuchs: Wiener med. Woch., February 8, 1903.
[112] Harlow Brooks: Archives of Neurol. and Psychol., i, p. 435, 1898.
[113] Cyon: Arch. de physiol., x, p. 618, 1898.
[114] Masay: *Loc. cit.*

lyzer; it is found in all tissues, in the female as well as in the male; it gives crystals of hæmin with Florence's test, etc., and other reactions peculiar to the adrenal and thyroid principles—both of which are also found in all tissues. A close examination of Masay's report, moreover, does not sustain his opinion that the rise of blood-pressure is to be ascribed to a secretion produced by the pituitary. The rise of pressure was *instantaneous* and general—a fact which points either to vasoconstriction through nerves or to the action of some intensely active and evanescent principle. Both these factors are available. Not only is the pituitary known to be related with the sympathetic system, but Langley[115] has called attention to the remarkable fact that "the effects produced by adrenalin upon any tissue are such as follow excitation of the sympathetic nerve which supplies the tissue," a conclusion confirmed by several observers. This paradoxical fact is clearly explained by the presence of the adrenal principle in the hæmoglobin. When Cyon and Masay excited the pituitary, therefore, they merely caused sympathetic constriction of all arterioles, including their offshoots the vasa vasorum; the walls of all vessels receiving an excess of albuminous hæmoglobin (adrenoxidase) they contracted, thus causing a rise of blood-pressure.

Again, as is well known, the adrenals are intimately connected with the abdominal ganglia and are, embryologically, sympathetic structures. Their vessels being likewise influenced, a sudden excess of secretion furnished a second cause for the ephemeral rise of blood-pressure observed by Masay. The power of the adrenal secretion to cause such a rise is generally recognized. Schäfer[116] characterizes as "astounding" the minuteness of the dose of adrenal extract that will excite physiological effects; 5.7 millionths of a gramme of Abel's epinephrin sulphate to each kilo of body weight was found by Reid Hunt[117] to cause a rise of blood-pressure of 66 mm. Hg. As to the action on the heart, Oliver and Schäfer[118] found, as is well known, that adrenal products not only acted directly on the muscular walls of blood-vessels, causing them to contract (which accounts for the rise of

[115] Langley: Hill's Recent Advances in Physiology, p. 584, 1906.
[116] Schäfer: Textbook of Physiology, i, p. 957, 1898.
[117] Reid Hunt: Amer. Jour. of Physiol., v, p. 7, 1901.
[118] Oliver and Schäfer: Jour. of Physiol., xvi, p. 1, 1894; xvii, p. 9, 1895

blood-pressure), but also upon the muscular wall of the heart. Finally, the rise of pressure is undoubtedly produced by the adrenalin extract itself, for Strehl and Weiss[119] found that clamping of the adrenal veins lowered the blood-pressure, while release of these vessels restored it to its previous level.

Another suggestive fact attesting to the pituitaro-adrenal parallelism is that

The pituitary, in keeping with the adrenals, gives rise to glycosuria.

Adrenal extractives, as observed by Blum,[120] Croftan,[121] Metzger,[122] Herter, and others, cause glycosuria. The adrenal secretion evidently provokes the phenomenon also, for Herter and Wakeman[123] found that compression of the adrenals, by increasing the outflow of secretion into the adrenal veins, caused glycosuria, while, conversely, adrenalectomy was followed by a marked diminution of the sugar in the blood. Again, we have seen that the adrenal secretion passes from the adrenal veins into the inferior vena cava; Kauffmann[124] found that when this great vessel was ligated the sugar diminished rapidly, both in the blood and in the urine.

Now, the influence of the pituitary over glycosuria is quite as marked. M. Loeb[125] urged, over twenty years ago, that the glycosuria which accompanies so often tumors of the pituitary should not be ascribed to mere coincidence. Marie observed it in over one-half of his cases of acromegaly. Borchardt[126] tabulated 176 patients with this disease, 71 of whom had glycosuria; as I had five years earlier,[127] he ascribes this symptom to overactivity of the pituitary, and its cessation to final degeneration of this organ. In 16 reported cases studied by Launois and Roy[128] each subject presented at the autopsy a tumor of the pituitary. That the glycosuria is not due to pressure of the enlarged organ upon the basal or bulbar tissues is shown by the fact that it can be produced in a normal organ. Thus, F. W. Pavy[129] found that,

[119] Strehl and Weiss: Pflüger's Archiv, lxxxvi, p. 107, 1901.
[120] Blum: Deut. Archiv f. Med., lxxi, Nos. 2 u. 3, p. 146, 1901.
[121] Croftan: American Medicine, January 18, 1902.
[122] Metzger: Münch. med. Woch., xlix, p. 478, 1902.
[123] Herter and Wakeman: Amer. Jour. Med. Sci., January, 1903.
[124] Kauffmann: Arch. de physiol., viii, p. 150, 1896.
[125] Loeb: Centralbl. f. inn. Med., September 3, 1898.
[126] Borchardt: Zeit. f. klin. Med., lxvi, No. 4, 1908.
[127] Sajous: *Loc. cit.*, i, p. 366, 1st edition, 1903.
[128] Launois and Roy: C. r. de la Soc. de biol., lv, p. 382, 1903.
[129] Pavy: Proc. Royal Soc. of London, x, p. 27, 1859.

"of all the operations on the sympathetic of the dog that have yet been performed, removal of the superior cervical ganglion the most rapidly and strongly produces diabetes." This enigmatic result finds its explanation in the light of the conclusions I have submitted: The superior cervical ganglion, as is well known, supplies vasoconstrictor filaments to the pituitary; removal of this ganglion by causing relaxation of its arteries causes the organ to become hyperæmic and therefore overactive, with glycosuria as a result. Control of this conclusion is afforded by the fact that, as in all exacerbations of activity thus induced, the symptom was fleeting, as shown by Pavy's statement that the glycosuria was "only of a temporary nature."

Having now ascertained 1, that the pituitary could alone be the source of impulses to the adrenals; 2, that this organ projected fibers toward the bulb, and, 3, that the pituitary and the adrenals gave rise to similar experimental and clinical phenomena, it became a question whether a nerve-path actually united these organs. Study of this question showed that

The phenomena provoked by both the pituitary and the adrenals can be traced by irritation or sections along a continuous path leading from the pituitary to the adrenals.

The tuber cinereum, which, we have seen, receives fibers from the pituitary, extends backward toward the bulb. Punctures along the upper part of this path by Ott, Tangl, and others not only raised the temperature and quickened the respiration, but a section below the same region by Sawadowsky[130] and Ott and Scott[131] rendered impossible the production of fever by agents known to produce it. Caselli,[132] moreover, found that irritation of the same tissues produced glycosuria.

The nerve-path continuing downward, we meet in the pontobulbar region the thermogenic center of Tscheschichin, Schreiber, and Reichert. Suggestive in this connection is the fact that Bruck and Günther[133] found that simple puncture with a probe between the pons and medulla not only caused a marked rise of temperature, but that this rise was general. The respiratory center is a familiar classic feature of the medulla; we have

[130] Sawadowski: Centralbl. f. d. med. Wissen., xxvi, pp. 145, 161, 1888.
[131] Ott and Scott: Jour. of Exper. Med., November, 1907.
[132] Caselli: *Loc. cit.*
[133] Bruck and Günther: Arch. f. d. ges. Physiol., iii, p. 578, 1870.

seen how all the phenomena evoked by the adrenals are linked with the respiratory process. All this applies as well to Claude Bernard's puncture in the same region as a cause of glycosuria, and due in the light of all this evidence to irritation of the path from the pituitary to the adrenals.

In the upper portion of the spinal cord, division by Tscheschichin,[134] Bernard,[135] and Pochoy,[136] respectively, in various animals sent the temperature down 7° to 16° C. in from four to twenty-four hours, death following in Pochoy's animals. Riegel[137] found that production of heat was diminished. That glycosuria is produced through efferent fibers passing downward in the upper cord is shown by the well-known fact, mentioned by Stewart,[138] that puncture of the bulb does not cause glycosuria if "the spinal cord above the third or fourth dorsal vertebra be cut before the puncture is made."

This level of the cord is of special interest, since it is here that the nerve-path to the adrenals leaves the spinal cord. Here can be evoked a rise of blood-pressure occurring in excess of that due to vasomotor nerves. Thus, François-Franck and Hallion[139] obtained a rise of pressure by exciting the five upper dorsal rami, and also by stimulating the corresponding segment of the sympathetic chain, although the vasoconstrictor nerves to the organ studied, the liver, was known to reach this organ through a lower ramus, the sixth—a limit confirmed by Langley.[140] But they could not account for this phenomenon. Bulgak, Bunch,[141] Jacobi,[142] and others also obtained marked vasoconstrictor effects by exciting these upper rami, although the vasomotor nerves to the organs influenced were known to leave the cord lower down. In other words, a duplicate source of vasoconstriction, as it were, was present whose nature remained obscure. It was brought to light, however, by the fact that Jacobi[143] found that excessive *inhibitory constriction of the intestinal vessels ceased,* and was replaced by normal vasoconstriction when he severed the nerves

[134] Tscheschichin: Arch. f. Anat., Physiol., u. wissensch. Med., p. 151, 1866.
[135] Bernard: Leçons sur la chaleur animale, p. 161, 1876.
[136] Pochoy: Thèse de Paris, 1870.
[137] Riegel: Archiv f. d. ges. Physiol., v, p. 629, 1872.
[138] Stewart: Manual of Physiology, p. 452, 1900.
[139] François-Franck and Hallion: Arch. de physiol., viii, No. 5, p. 936, 1896.
[140] Langley: Schäfer's Textbook of Physiology, ii, p. 644, 1900.
[141] Bunch: Jour. of Physiol., xxiv, p. 72, 1899.
[142] Jacobi: Arch. f. exper. Path. u. Pharmakol., xxix, p. 171, 1892
[143] Jacobi: *Ibid.*

to the adrenals. The intense action of their secretion on the blood-pressure clearly accounts, from my viewpoint, for the excessive constriction observed.

Briefly, these facts indicate jointly that

The pituitaro-adrenal path leaves the spinal cord through the upper four or five rami, to enter the sympathetic chain, and then the great splanchnic, which, through the intermediary of the semilunar ganglia, supplies nerves to the adrenals.

That this path is the true one is shown by additional data. Thus, Goltz and Ewald[144] found that animals deprived of their spinal cord from the bulb down could live a long time—years even—but that they showed a striking peculiarity, even after their vessels had resumed their normal caliber, that of dying of cold. Ott[145] found, however, that the animals were able to generate their usual heat when the section was made *below* the fifth dorsal vertebra. This is evidently because the pituitaro-adrenal nerve-paths had left the cord above this level to pass over to the sympathetic chain and the splanchnic, for, although Biedl[146] had failed to increase the secretory activity of the adrenals by exciting electrically all the median and lower dorsal rami, both he and Dreyer[147] had succeeded in doing so by stimulating the great splanchnic nerve. Proof of this is afforded by the fact that the greater splanchnic also transmits impulses to the adrenals which provoke glycosuria, for Laffont[148] caused it by stimulating this nerve. Moreover, it is evidently through a nerve-path starting at least in the medulla that glycosuria is caused; for Eckhard, Kauffmann,[149] and others found that even the glycosuria caused by Bernard's puncture ceased when the greater splanchnic was severed. There can be no doubt that it is through the adrenals that the glycosuria is caused, for, besides the evidence I have already adduced to this effect, A. Mayer[150] found that Bernard's puncture failed to produce this symptom after removal of the adrenals.

On the whole, all the evidence, of which the foregoing is a part, seems to me to have shown:—

[144] Goltz and Ewald: Archiv f. d. ges. Physiol., lxiii, pp. 362, 400, 1896.
[145] Ott: Textbook of Physiology, p. 348, 1904.
[146] Biedl: Arch. f. d. ges. Physiol., lxvii, No. 9-10, p. 443, 1897.
[147] Dreyer: Amer. Jour. of Physiol., ii, p. 203, 1899.
[148] Laffont, cited by Laulanié: Eléments de physiologie, 2d ed., p. 943, 1905.
[149] Kauffmann: C. r. de la Soc. de biol., p. 284, 1894.
[150] Mayer: Arch. gén. de méd., July 17, 1906.