

PREFACE TO THE SEVENTH EDITION.

ALTHOUGH the last edition of the present work was published less than two years ago, a new edition has become necessary owing to the vast amount of labor contributed to the study of the internal secretions during the last two years by the profession at large. Notwithstanding this widespread scrutiny into the scientific aspects of the subject, the author is pleased to note that the views formulated by himself in preceding editions concerning the functions of the ductless glands are increasingly being sustained by the researches of other investigators and clinicians. Even some of the apparently unwarranted conclusions submitted as far back as 1903, such as the presence of the adrenal principle in the nervous elements, the joint participation of the various ductless glands in the immunizing functions of the body, the identity of the adrenal system as that upon which shock, fright, etc., react, the identity of leucocytes as intermediaries for the transmission of digestive ferments to the tissue cells and blood for defensive purposes, etc., have received sufficient and independent support to warrant their early adoption as fixed facts.

In the present edition much of the introductory matter submitted in preceding editions as foundation for the views introduced has been replaced by the application of these views to the practical field. Thus, the pathogenesis of exophthalmic goiter and goiter no longer remains within the field of conjecture when, with the writer, the cause of these disorders is not restricted to a single factor,—whether water borne, auto-intoxication, etc.,—but to a multiplicity of factors, all of which can provoke a defensive reaction of the thyroid apparatus, with hyperplasia of the thyroid, besides, in exophthalmic goiter, a systemic reaction. A logical foundation for successful treatment, including newer measures recently introduced, operative removal, etc., are thus afforded. The vast subject of mental deficiency in childhood, including that witnessed in backward

children, shown recently to include 20 per cent. of the pupils of our public schools, is another notable addition. The intimate causal relationship of the thymus gland in this connection is introduced not only as an elucidative factor, but as the foundation for a rational use of organotherapeutic agents. The part played by each of the various ductless glands in idiocy and the stigmata indicating deficiency of each of these organs have also been introduced with the same end in view. The prophylaxis of mental deficiency is another new feature of the present edition. The mother and infant are shown to be the fruitful field for protective measures, *i.e.*, before the plastic brain of the offspring has had time to develop abnormally.

The subject matter of the work has also been revised and, where deemed of interest to the reader, enriched with newer facts. Among these subjects may be mentioned the chromaffin system, the functional relationship between the kidneys and the adrenal system, and the internal secretion of the former. The generative glands of both sexes are studied from a new standpoint, both as regards the functions of their internal secretions and the influence of the ductless glands on sex characteristics. The section on organotherapy has also been revised, the subjects which are now receiving attention, corpus luteum and pituitary products, having been practically rewritten.

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PREFACE TO THE SECOND AND THIRD EDITIONS.

(Containing a summary of the author's newer conceptions up to 1907.)

WHILE the manuscript for the first volume was delivered to the publishers in 1902, the second volume was only finished in 1907. As the latter embodied researches carried on during the interval of five years between the two volumes, it became necessary to correct what errors the first contained in the light of these researches. This feature, coupled with the large patronage the medical profession has granted the work, has imposed the need of new editions. That very few corrections have proven necessary, either by reason of these investigations or of what justified criticisms the work has received, is shown by the list of additions to our knowledge (see page x *et seq.* of this preface) it introduces. The second volume may thus be said only to amplify the newer functions I pointed out in the first volume in 1902 and to illustrate their importance in practice.

The present status of Medicine precludes any apology for the publication of a work such as this. Professor Sollmann, a prominent member of the Council of Pharmacy of the American Medical Association, wrote, only recently (1908): "A generation ago therapeutics was an art, promising to develop into a science. At present it cannot be classed as an art, nor as a science; it can only be classed as a confusion." Indeed, Osler's public declaration¹ that of the action of drugs "we knew little" though we "put them into bodies the action of which we know less," sustained by Llewellys F. Barker's estimate published about the same time,² "that drugs of *unknown* physiological action cannot *conscientiously* be set to act upon bodily tissue in disease in which we are ignorant of *deviations from the normal*," involves the conclusion that our ignorance applies to disease as well as to therapeutics—in a word, to all that which endows us with the right to accept, with any degree of self-respect, the confidence which suffering humanity places in us.

It is not my purpose to take issue with these frank ex-

¹ Osler: N. Y. Sun, Jan. 27, 1901.

² Llewellys F. Barker: Bull. Johns Hopkins Hosp., July-Aug., 1900.

pressions of opinion. In fact, were I to do so, I would conceal similar conclusions reached nearly twenty years ago, when, as editor of the "Annual of the Universal Medical Sciences," it became my lot to collate, with the valued collaboration of many associates, the multitude of data, clinical and experimental, which were accumulating from year to year. Nor do they conflict with the prevailing estimate of the therapeutic worth of Medicine among the best-informed medical men abroad. Skoda's dictum of several years' standing, "that we can diagnose disease, describe it, and get a grasp of it, but we dare not expect by any means to cure it," has drifted along, on the ripples of time, until, hardly two years ago (1907), the president of a prominent British society, Dr. A. H. Brampton,³ found it opportune to declare that "if any daring member has introduced a subject bearing on medical treatment, it has been with an apologetic air and humble mien, well knowing that if his remarks had any reference to the utility of drugs in the treatment of disease they would be subjected to good-humored banter, and received by those sitting in the seat of the scornful with amused incredulity." My aim now, as it was when "Internal Secretions" was first projected, is to indicate what to me, at least, appears to be the main cause of the deplorable state of practical Medicine, and if possible to eliminate it.

When, twenty years ago, I was brought face to face with the mass of heterogeneous material we term the "Medical Sciences," and with the yearly crop of contradictory theories upon each disease, mode of treatment, etc., I soon realized that some gigantic flaw could alone account for so great a confusion. In the preface of the 1888 issue, I had stated that the "Annual" was intended "to become a helpmate to the practitioner in his efforts to relieve suffering, and to assist the investigator by correlating facts, thus enabling him the better to compare." Whether much comparison was indulged in by others I cannot say, but the fact remains that, as far as my own position in the matter was concerned, I began then and there to seek for the flaw referred to. I must frankly confess that its identity was not difficult to find, namely: the invalidity of Physiology. Never, when it came to tracing a pathological condition,

³ A. H. Brampton: *Lancet*, Jan. 19, 1907.

the effect of a remedy, the nature of a symptom, or any, in fact, of the many phenomena which to us practitioners are of paramount importance in diagnosis or therapeutics, was it possible to trace to its source the chain of events through which a normal function had more or less suddenly become abnormal. Invariably was it found that either the physiologists had failed altogether to discern the nature of that function, or, if an attempt had been made by them to explain it, that it was laden with so many inconsistent and obviously mutually contradictory conclusions that—although perhaps quite scientific in their eyes—it was more misleading than helpful in the explanation of the morbid condition analyzed.

To illustrate these statements, I will submit a few of the more salient deficiencies referred to. The process of respiration, which includes pulmonary respiration and oxygenation of the blood and tissues, at once asserts itself as of capital importance, since it involves the functions of all organs, the vital process, and also every morbid process. In January, 1903, I urged that this function as taught by physiologists failed to satisfy our needs, and suggested new paths for research. Two years later, Professor Chas. R. Barnes, of the botanical department of the University of Chicago,⁴ wrote: "I found it needful to examine the recent literature of respiration in animals, the aspect of the general subject with which I felt myself least familiar. I found to my great surprise, that animal physiologists have concerned themselves very little with the essential problems of respiration." Then, naming our best-known text-books on physiology, he added: "I found no treatment whatever, indeed, no mention whatever, of the real problems of respiration, that is, of what is happening in the tissues, the process of which these external phenomena are the sign." The late Sir Michael Foster⁵ also closed a study on metabolism in the last edition of his text-book with the statement that, after all, it "consists mostly of guesses and gaps." Even the apparently simple process through which the blood acquires its oxygen from the air in the pulmonary alveoli is at present unknown to physiologists, their gasometric experiments being,

⁴ C. R. Barnes: *Science*, Feb. 17, 1905.

⁵ Sir Michael Foster: cited by W. G. Little: *Liverpool Med.-Chir. Jour.*, Jan., 1905.

as stated by Pembrey,⁶ "very discordant" and inadequate to explain "the absorption of oxygen by the lungs."

If the full meaning of these deficiencies is apprehended, their appalling consequences will appear. The pulmonary air-cells are the main barriers to infection: their surface is the seat of multiplication of the pneumococcus, while their walls afford a nidus for the tubercle bacillus. It is here, therefore, that the initial lesions of the two great destroyers of mankind, pneumonia and tuberculosis, are formed. Now, adequate knowledge of the processes with which oxygen is concerned precisely in this location, would be a boon indeed: it would enable us probably to discern just how Nature defends the body against infection. As to the morbid processes connected with tissue respiration, I pointed out in the first volume,⁷ two years before Beard suggested its use as a remedial agent, that trypsin was the direct destructive agent in another dread disease, cancer. Trypsin is now known to take part in tissue-metabolism. If we had something better than the "guesses and gaps" referred to at our disposal to study this next greatest foe of humanity, I venture to suggest that it would soon be conquered.

Another great function is nutrition. Our first need to interpret intelligently gastro-intestinal infections, is a clear understanding of ferments. A most able physiologist, Benjamin Moore,⁸ wrote recently: "Little is known regarding the chemical nature of enzymes, because all attempts to isolate them in a state of purity have hitherto failed." Another authority, Halliburton,⁹ also writes: "The process through which the digested food-stuffs are absorbed from the alimentary canal is quite as obscure." Thus, Howell¹⁰ writes: "The energy that controls absorption resides . . . in the wall of the intestine, presumably in the epithelial cells, and constitutes a special form of imbibition which is not yet understood." According to Beddard,¹¹ "we know nothing of the path taken by the products of proteid and carbohydrate digestion." Howell¹² also

⁶ Pembrey: Schäfer's "T. B. of Physiol.," vol. i, p. 776, 1898.

⁷ Sajous: *Cf.* vol. i, pp. 609 to 666 incl., 1903.

⁸ Moore: Hill's "Recent Advances in Physiol., etc.," p. 117, 1906.

⁹ Halliburton: "Biochemistry of Muscle and Nerve," p. 30, 1904.

¹⁰ Howell: "T. B. of Physiol.," p. 713, 1905.

¹¹ Beddard: Hill's "Recent Advances in Physiol., etc.," p. 643, 1906.

¹² Howell: *Loc. cit.*, p. 716, 1905.

says: "The form in which proteid is absorbed remains . . . a mystery." Again, if, as text-books on physiology teach, the food-stuffs, duly prepared, were taken up at all by the blood, they should be found in the latter. But, as stated by Mendel,¹³ "Beyond the intestinal wall, in the blood and lymph-stream, the cleavage products seem, for the most part, to be missing." Finally, once in the blood, the fluid proteids should be readily diffusible to penetrate freely to the tissue-cell. Howell¹⁴ states: "The proteids of the blood, which are supposed to be so important for the nutrition of the tissues, are practically indiffusible, so far as we know. It is difficult to explain their passage from the blood through the capillary walls into the lymph."

The problem of nutrition is evidently no more solved by physiologists than those of respiration and tissue metabolism. The consequences to us are quite as deplorable. Asiatic cholera, typhoid, infantile diarrhoea, and kindred disorders are closely related with all intestinal functions, and in absorption lies the key-note to general infection. How can we possibly obtain a clear conception of all these dread diseases with such a foundation as physiology affords us?

The third great question is the manner in which function is incited in an organ. As shown by Claude Bernard, over fifty years ago, this is due to dilation of the arteries of that organ; more blood passing through it, it functionates. Notwithstanding considerable work done upon the problem ever since, the manner in which this function is carried out is quite unknown. Naturally, to admit more blood into an organ, the nutrient arteries must be dilated. Now, in his summary of vasomotor actions, Foster,¹⁵ for instance, says, referring to the presence of dilator nerves in muscles: "There is no adequate evidence that these vasodilator fibers serve as channels for tonic dilating impulses or influences." While Landois,¹⁶ in the last edition of his text-book, holds that "although a center for vasodilator or vessel-relaxing nerves has not yet been demonstrated, the existence of such a center in the medulla may nevertheless be suspected," J. G. Curtis¹⁷ states that "it is not known whether

¹³ Mendel: *Med. News*, May 20, 1905.

¹⁴ Howell: *Loc. cit.*, p. 886.

¹⁵ Foster: "T. B. of Physiol.," sixth American edition, p. 229, 1895.

¹⁶ Landois: "T. B. of Physiol.," tenth edition, p. 771, 1905.

¹⁷ J. G. Curtis: "Amer. T. B. of Physiol.," vol. i, p. 199, 1900.

a vasodilator center is present in the bulb." The actual state of the question is aptly summarized by H. C. Chapman,¹⁸ when he says: "Though numerous explanations have been offered of the manner in which the vasodilator nerves act, it must be admitted that none of them are satisfactory, and that it is not yet understood how this stimulation causes dilatation of the blood-vessels."

Now, the bearing of this physiological process upon pathogenesis and therapeutics may be said to be limited only by the total number of diseases to which the human frame is exposed, since all disorders are functional or organic, and all organic diseases impair function at a given time. A possible exception suggests itself, namely, the nervous system. But here, again, the *deus ex machina* of the function as a whole, the nerve-impulse, has remained hidden. As Landois¹⁹ says, "the nature of the physiological nerve-stimulus in the normal body is not known." This accounts for the prevailing discouragement among the devotees of a great specialty, neurology, as expressed in the recent statement of a very diligent worker in that line, Joseph Collins,²⁰ "that we know very little more concerning the etiology, pathogenesis, and the clinical display of the majority of nervous diseases, organic and functional, than we did twenty years ago."

These are but a few of the evident shortcomings of Physiology; others will be referred to in the body of the work. I wish to state, however, that their enumeration is not inspired by a spirit of criticism; they are mentioned because each deficiency is subjected to a searching inquiry in the second volume with a view to its elimination: Indeed, any one who has examined physiological lore as closely as I have, cannot but admire the enormous and patient labor that physiologists have devoted to the solution of the multitude of problems which the functions of the human organism involve, including the many unsolved ones to which I refer. But I must now, after writing the second volume, emphasize a feature which I merely suggested in the first volume, viz., that their failure to explain the many functions referred to is due to the fact that they have

¹⁸ H. C. Chapman: "Human Physiology," second edition, p. 692, 1899.

¹⁹ Landois: *Loc. cit.*, p. 631.

²⁰ Joseph Collins: *Monthly Cyclo. of Pract. Med.*, Feb., 1905.

overlooked the cardinal functions of the organs to which I have given special attention: the adrenals, the thyroid, the pituitary body and the leucocytes.

As the text will show, various branches of biology have been studied, but many of the facts which have served to elucidate function were obtained from clinical medicine. A great physiologist, Professor Pawlow, of St. Petersburg, wrote a few years ago,²¹ after stating that physicians had pointed out the existence of gastric secretory nerves—a question which, I may add, has been greatly elucidated, thanks to his own labors: "Physiologists, on the other hand, had fruitlessly endeavored for decades to arrive at definite results upon this question. This is a striking, but by no means isolated, instance where the physician gives a more certain verdict concerning physiological processes than the physiologist himself; nor is it indeed strange. The world of pathological phenomena is nothing but an endless series of the most different and unusual combinations of physiological occurrences which never make their appearance in the normal course of life. It is a series of physiological experiments which Nature and life institute, often with such an interlinking of events as could never enter into the mind of the present-day physiologist, and which could scarcely be called into existence by means of the technical resources at our command. Clinical observation will consequently always remain a rich mine of physiological facts." There are precedents, therefore, upon which a legitimate belief may be based that the conclusions I have reached are sound. They afford, moreover, a clear explanation of the inability of physiologists to discern the functions my researches have led me to discover: they are partly hidden in a field that physiologists could not legitimately be expected to scrutinize, owing to its vastness. In this connection, it is mainly, therefore, as a contribution of pathological biology to normal biology, of which physiology is a subdivision, that the two volumes of "Internal Secretions" are offered.

Among the more important features which the views I advance therein appear to me to point out for the first time

²¹ Pawlow: "The Work of the Digestive Glands," Thompson's transl., p. 46, 1902.

(as far as the literature and the experimental and clinical facts within my reach have enabled me to judge) are the following:—

As bearing directly upon Biology:—

1. The main function of the adrenals, viz., to supply an internal secretion which absorbs the oxygen of the air to carry it to the tissues; and, as a result of this fact:—
2. Pulmonary respiration, and
3. Tissue respiration;
4. The identity of the albuminous moiety of the hæmoglobin molecule, viz., the oxygenized adrenal secretion;
5. The identity of the oxidase of the blood, *i.e.*, the oxygenized adrenal secretion referred to (after the thirteenth chapter) as "adrenoxidase";
6. The identity of the red corpuscles as storage-cells for adrenoxidase and as purveyors of this body to the tissues;
7. The general composition of ferments;
8. That the adrenal principle is the one ferment which endows all other body-ferments with their properties as such;
9. The identity of "secretin" as adrenoxidase;
10. The identity of "enterokinase" as adrenoxidase plus nucleoproteid;
11. That the granulations of the leucocytes serve to build our tissues and to nourish them;
12. That the substances out of which the leucocytes form their granulations (anabolism) are the proteids and carbohydrates ingested by them in the intestinal canal, its epithelium and villi, and in the blood; And, in virtue of these facts:—
13. The process of absorption, and
14. The process of general nutrition;
15. That it is the function of leucocytes to convert the constituents of the ingested proteids into living proteids;
16. That the granulations they supply to the tissue-cells are living substance;
17. That the principle which endows the constituents of proteids with life in the leucocytes is the adrenal active principle;
18. That the adrenal principle is the dynamic element in the vital process;
19. That the granulations of leucocytes once in the tissue-cells live temporarily therein and are, when worn, broken down by ferments (catabolism), and voided by the cellular vacuoles into the pericellular lymph-spaces; And, in virtue of the foregoing conclusions:—
20. The process of metabolism;
21. That all the ferments and carbohydrates found in the tissues and other immobile cells are brought to them by leucocytes and are derived from the alimentary system, especially the pancreas (trypsin) and liver (glycogen);
22. That a portion of the pancreatic ferments forms an internal secretion which passes to the splenic vein and thence into the portal system;
23. That the splenic internal secretion (probably nucleo-proteid) also passes out into the splenic vein and thence into the portal system;
24. That on reaching the portal system from the alimentary canal, the leucocytes absorb the pancreatic ferments and splenic internal secretion (probably nucleo-proteid) which they supply to the tissue-cells and with which they carry on their intrinsic functions;

25. That the nervous system, in keeping with other tissues, is composed of cells likewise developed and nourished by leucocyte-granulations, and traversed by the oxygen-laden adrenoxidase;
26. That the ground substance and Nissl granules of nerve-cell-bodies and the myelin of their axis-cylinders or nerves are to the nerve-cell what the cytoplasm is to other tissue-cells;
27. That the neuro-fibrils, including those of the axis-cylinders, are nerve-capillaries through which the nerve-cells are supplied with oxygen-laden adrenoxidase;
28. That these neuro-fibrils receive their adrenoxidase-laden plasma from the general circulation through the intermediary of the neuroglia fibers (also capillaries) and the neuroglia-cells which regulate the volume of plasma admitted into the neuroglia fibers; And, in virtue of the last four conclusions:—
29. The circulation of the nervous system;
30. That the myelin of nerves is not a mere insulating material or sheath, but a compound rich in phosphorus which, when in contact with the oxygen-laden adrenoxidase circulating through them, generates nerve-energy;
31. That the ground-substance, the Nissl granules and the myelin in the cell-bodies of neurons and their dendrites, are also phosphorus-laden compounds which, when in contact with the adrenoxidase circulating through them, generate nerve-energy; And, in virtue of the last two conclusions:—
32. The source and nature of the nerve-impulse;
33. That the pituitary body is the general and governing center of the spinal system, which includes the gray substance of the base of the brain, pons, bulb and spinal cord, and the nerves derived from any of these structures, cranial or spinal, though subsidiary centers are also present in the bulb and spinal cord;
34. That the pituitary body is the governing center of all vegetative functions, *i.e.*, the somatic brain; And, in virtue of these two conclusions:—
35. The identity of the pituitary body as the most important of all organs concerned with the vital functions of invertebrates and vertebrates, including man;
36. That the brain (as differentiated from the somatic brain) is the organ of mental processes and not the governing organ of motor functions; though capable, through the voluntary impulses it transmits to the spinal system, of having its mandates carried out; And, in virtue of these two conclusions:—
37. The identity of the brain (as differentiated from the somatic brain) as solely the organ of Mind.
38. That neither the anterior nor the posterior pituitary body is a secreting gland;
39. That the anterior pituitary body is a lymphoid organ which, through the intermediary of a center located in the posterior pituitary body and a nerve-path in the spinal system, the upper dorsal sympathetic ganglia and the splanchnic nerves, governs the functional activity of the adrenals; And, in virtue of this conclusion:—
40. That the anterior pituitary body governs, through the posterior pituitary body, all the oxidation processes of the body;
41. That the center in the posterior pituitary body through which the anterior pituitary body governs the adrenals also controls the functional activity of the thyroid gland, and thus constitutes the "adrenothyroid" center;
42. That the pituitary body, the adrenals and the thyroid gland (including the parathyroids) are thus functionally united, forming the "adrenal system;"

43. That the posterior pituitary body is the seat of the highly specialized centers which govern all the vegetative or somatic functions of the body, and of each organ individually;

44. That the posterior pituitary body receives all the sensory impressions belonging to the field of common sensibility: pain, touch, muscular sense, etc., initiated in any organ, including the mucous membranes, skin and brain;

45. That owing to this fact, the posterior pituitary body is the *sensorium commune* upon which all emotions, shocks—psychical or traumatic—concussions, etc., react, the resulting impairment of its functions being the cause of the morbid phenomena observed under such conditions;

46. That the sympathetic system is also governed by a center, and

47. That the sympathetic center is likewise located in the posterior pituitary body and constitutes one of the most sensitive of its centers;

48. That it is the function of the sympathetic center and of the sympathetic system to govern the caliber of all arterioles, and to regulate, through the spiral muscular coat of these vessels, the volume of blood admitted into the capillaries of any organ, including those of the brain and nervous system;

49. That the vasomotor center governs the caliber of the larger vessels only, *i.e.*, of all vessels that are larger than the arterioles;

50. That active vasodilation exercised through vasodilator nerves is limited to the arterioles;

51. That dilation of an arteriole is due to constriction by the terminal fibers of a cranial nerve (the vagus, for example) of the vasa vasorum which supply its walls with adrenoxidase-laden plasma, thus causing ischæmia and relaxation of its muscular coat;

52. That while this process, "stricto-dilation," serves to admit an excess of blood into an organ when the functional activity of the latter is to be increased, the sympathetic fibers, when the organ's functions are to cease, restore the arterioles to their normal caliber;

And, in virtue of the facts embodied in the last seven conclusions:—

53. The mechanisms of vasodilation and function.

As bearing directly upon Immunity:—

54. That the sensory organ in the partition between the two lobes of the pituitary body is morphologically the homologue of the "test-organ" or "osphradium" of mollusks and other Invertebrates, which has for its purpose to protect the animal against noxious materials that may be present in the water admitted into its organism;

55. That all Vertebrates, including man, are protected, as are Invertebrates, against noxious materials that may be present in the blood (a chemical homologue of sea-water), their test-organ, a sensory structure, being sensitive to certain poisons as the olfactory area, which it resembles histologically, is to odors;

56. That the test-organ of Vertebrates, including man, reacts under the influence of any poison brought to it by the blood or its leucocytes (phagocytes) capable of exciting it, by increasing, through the adreno-thyroid center, which it governs, the functional activity of the adrenals and of the thyroid and parathyroids;

57. That by increasing the functions of the adrenals it enhances the bacteriolytic and antitoxic powers of the blood and its phagocytes;

58. That by increasing the functional activity of the thyroid and parathyroids it increases, through their secretions, the sensitiveness of all cells, including bacteria, and their vulnerability to phagocytes, inasmuch as

59. The secretions of the thyroid and parathyroids jointly form the opsonin and agglutinin of the blood;

And, in virtue of the last six conclusions:—

60. That the adrenal system, composed of the pituitary body, the adrenals and the thyroid apparatus, constitutes the immunizing mechanism of the body; and, furthermore,

61. That inasmuch as the adrenal system has for its purpose to protect the body against disease, it is by enhancing the functional activity of the adrenal system that we can overcome disease;

62. That the adrenal system causes the appearance, in the blood and phagocytes, of an excess of "auto-antitoxin," a (qualitative) chemical homologue of diphtheria antitoxin and other antitoxins;

63. That this "auto-antitoxin" (as well as all other antitoxins) is composed of the internal secretions of the adrenals (adrenoxidase: Ehrlich's amboceptor), of the pancreas (trypsin: Ehrlich's complement), of the spleen and leucocytes (nucleo-proteid), and of the thyroid and parathyroids (thyroidase: Wright's opsonins);

64. That it is to the excess of auto-antitoxin that the increased bacteriolytic and antitoxic properties of the blood and phagocytes (the true *vis medicatrix naturæ*) are due.

As bearing directly upon Pharmacodynamics:—

65. That rational Therapeutics, in so far as the cure of pathogenic processes based on toxæmias is concerned, should include measures which promote the formation of auto-antitoxin in the blood and phagocytes;

66. That we have drugs, of which thyroid extract, mercury, and iodine are types, which provoke energetically the formation of auto-antitoxin;

67. That the production of an excess of auto-antitoxin in the blood, under the influence of bacterial toxins or endotoxins, or of any poison capable of exciting the test-organ (and through it the adrenal system) sufficiently, is the phenomenon known as "fever," and that the "thermogenic" or "heat" center is thus located in the pituitary body;

And, in virtue of this conclusion:—

68. The nature of fever and its mode of production;

69. That we can by means of agents which stimulate concomitantly the test-organ and the vasomotor and sympathetic centers or any two of these centers, enhance metabolism and nutrition and the production of auto-antitoxin, as exemplified by belladonna, strychnine, coca, quinia and other drugs;

70. That we can supply the body with the constituents which its blood and tissues lack and that these agents are adjusted to the needs of each organ by the leucocytes, as exemplified by iron and phosphorus;

71. That all drugs are taken up by leucocytes in the intestinal canal and blood and transported by them to all parts of the body;

72. That the sympathetic center in the posterior pituitary body is the sleep center;

73. That the sympathetic center provokes sleep by lowering the functional activity of the anterior pituitary body and of the adrenal system, and causes thereby a general relaxation of all arteries, accumulation of blood in the splanchnic area, and ischæmia of the cerebro-spinal system;

74. That drugs of which opium is the type, produce sleep by stimulating the sympathetic center;

75. That drugs of the type of chloral, the bromides, etc., produce sleep by depressing the vasomotor center and causing accumulation of blood in the splanchnic area and ischæmia of the cerebro-spinal system;

And, in virtue of the four last conclusions:—

76. The manner in which sleep is provoked;
77. That anæsthetics of which chloroform and ether are types, produce sleep and anæsthesia by exciting powerfully the vasomotor center, causing thereby general vasoconstriction followed by hyperæmia of all capillaries, including those of the cerebro-spinal system, and venosity of their arterial blood;

78. That anæsthetics of which nitrous oxide is a type, produce sleep and anæsthesia by replacing the oxygen of the air and producing venosity of the blood in the capillaries of the cerebro-spinal system and other organs;

79. That pain is due to hyperæmia of the sensory-nerve terminals, of the *nervi nervorum*, etc., and that any agent which indirectly or directly causes diminution of this hyperæmia counteracts pain;

And, in virtue of this conclusion:—

80. The nature and mode of production of pain;

81. That analgesics of the type of opium counteract pain by stimulating the sympathetic center, and by thus causing the dilated arterioles which supply the painful area to resume their normal caliber;

82. That analgesics of the type of antipyrin, acetanilid, etc., counteract pain in the same way, but, being more violent in their action, are apt to cause hyperconstriction of the arterioles and cyanosis;

83. That drugs of the type of amyl nitrite, nitroglycerin, etc., produce dilation of the arterioles by inhibiting the functional activity of the sympathetic center;

84. That drugs of the type of *veratrum viride*, the bromides, etc., lower the vascular pressure by inhibiting the functional activity of the vasomotor center;

85. That alcohol is a fictitious stimulant and in reality a depressant, owing to the fact that it deoxidizes the plasmatic adrenoxidase;

86. That the mineral salts fulfill so important a rôle in the preservation of the osmotic properties of the body fluids and their alkalinity, that their replacement in all diseases in which they are actively reduced is an essential feature of the curative process;

87. That purgatives produce their beneficial effects by causing either reflexly or by centric action, according to the purgative used, an increase of bacteriolytic and antitoxic auto-antitoxin in the intestinal canal;

88. That all emetics produce their effects by provoking irritation of the gastric mucosa: the local emetics (mustard, zinc sulphate, etc.) by irritating it directly; the general emetics (apomorphine, tartar emetic, etc.) by depressing markedly the vasomotor and sympathetic centers and thus causing dilation of the arterioles and hyperæmia of the gastric glandular elements;

89. That diaphoretics act similarly, the sweat glands (as well as all other glands) being rendered hyperæmic and overactive.

Bearing directly upon Pathogenesis and Therapeutics:—

90. That the vulnerability of the organism to infection is inversely proportional to the efficiency of the adrenal system, the relative amount of auto-antitoxin in the pulmonary and intestinal secretions, and the bacteriolytic activity of the phagocytes;

91. That the diseases which are most fatal to mankind: cancer, tuberculosis, pneumonia, Asiatic cholera, bubonic plague, etc., are due to agencies, endogenous or exogenous, which interfere with, or paralyze, the functions of the test-organ and through it the adrenal system;

92. That all these diseases can be treated successfully, when seen not too late, by means of remedies which excite with adequate activity

the test-organ, and provoke through it an accumulation of auto-antitoxin and thyroidase (opsonin) in the blood;

93. That the convulsive diseases: tetany, tetanus, epilepsy, puerperal eclampsia and rabies, are all due to the accumulation of toxic waste-products in the blood;

94. That all these convulsive diseases can be arrested by measures which prevent the accumulation of toxic wastes in the blood and which increase the proportion of auto-antitoxin in the latter,—provided organic lesions in the cortex (gliosis) have not been given time to develop;

95. That all the diseases grouped under "gouty diathesis:" gout, migraine, neuralgia, sciatica, etc., are due to hypoactivity of the test-organs and the adrenal system;

And, in virtue of these six conclusions:—

96. That the most fatal and distressing diseases of mankind have not been mastered because the cardinal rôle of the adrenal system in their pathogenesis, prevention and cure, has been overlooked.

As previously stated, this list includes only the more important functions that my researches—including personal investigations in the laboratory, clinical observations, and analysis of the vast fund of knowledge available in literature—have brought to light. Were all enumerated, including those introduced in the departments of "Pharmacodynamics" and "Pathogenesis and Therapeutics" (where they are designated by asterisks in each drug and disease studied), they would aggregate several hundred. This fact is only referred to in order to illustrate the far-reaching importance of the functions of the internal secretions in all processes, normal, morbid, or protective, and the large number of gaps they fill.

The final conclusions to which I have been led—those submitted in the second volume—are not offered as mere theories, but as solutions carefully worked out from the abundant material at my disposal. My labors as editor of the "Annual of the Universal Medical Sciences" and the "Cyclopædia of Practical Medicine" having shown that it was to the habit of theorizing with a few facts as foundation into which investigators, and particularly laboratory workers, have fallen, that the confusion which characterizes the Medicine of our day was due, the following working plan was adopted: The literature of each subject, my own experimental and clinical observations, etc., were collected, subdivided and filed. When a given subject was taken up, each paper available was analyzed and the sound experimental or clinical facts or observations were noted and arranged in series. In physiological questions, the teachings of physiological botany, zoölogy and cytology were added. All

these data (amounting to several hundreds in some instances) were treated as factors in the search of a solution—the solution submitted at the end of each section, in italics in the first seventeen chapters, and thereafter in large type. The final solution reached in each instance was submitted to a rigid test, however, viz., *absolute concordance with all other solutions in the work*—a process which brought to light any defect, not only in the solution itself, but likewise in all conclusions previously adduced. The chances of error were thus reduced to a minimum, while a solid framework was elaborated for future discoveries by other investigators.

These details are given not only with the object of aiding others who might wish to work on parallel lines, but to illustrate another salient feature brought to light by my editorial work upon the "Annual" and the "Cyclopædia," namely, that *the present unsatisfactory condition of Medicine is due to the fact that investigators do not avail themselves of the enormous array of solid data available to ascertain the truth*. Blinded by the fallacious idea that the worth of a contribution to our knowledge should be gauged solely by the new experiments and clinical observations it adds to those already available, they lose sight of the fact that such experiments and observations are but bricks and mortar out of which a coherent and truly useful Medicine—one indeed worthy of ranking as a science—can be built.

The conception of Medicine presented in the second volume—and foreshadowed in the first—is submitted only as an *effort* in this direction. It aims to replace the empirical and hazardous use of remedies which has undermined increasingly the confidence of our best observers in them, by a system of therapeutics based on solidly established facts which makes it possible to trace every phase of their action to its source. The centers influenced may thus be used by the physician as so many levers through which he can regulate the defensive agencies of the organism and the mechanisms which distribute them, precisely as a general can govern the defensive movements of an army in the field. As the disease-causing substances, toxins, endotoxins, toxic wastes, etc., are also shown to produce their effects through a morbid action upon the centers influenced by our remedies, they may thus be met directly where they strike and antagonized before they can destroy life.

The work introduces no elixir of life, no universal panacea, nor even a new serum, the weapons recommended are available to all, viz., the identical remedies which for years have been in daily use—the forty or fifty that have stood the test of time. It shows, I believe, that it is not because we have been lacking agents capable of successfully coping with disease that confidence in remedies has been steadily decreasing, but because they were used blindly and often, therefore, injudiciously. There is now not the least ground for doubt as to the efficiency of our therapeutic resources. I shall be amply repaid if I have succeeded in proving this fact, and if "Internal Secretions" to any degree instills into its readers the unbounded confidence in the power of our remedies to antagonize and even master disease that a broad survey of the scientific facts at our disposal and considerable practical experience have instilled into me.

The plan of the second volume, as stated in the preface, included only "Applied Therapeutics," *i.e.*, the physiological action of drugs in morbid processes, but thanks to the liberality of my publishers, the F. A. Davis Company, I was able to add a department in which the pathogenesis and treatment of the most fatal and distressing diseases with which we have to contend are treated in full. Hence the comparatively large size of the second volume.

It is with great pleasure that I acknowledge the encouragement and moral support I have received during the rather arduous task the preparation of this work imposed upon me, from my friends, Mr. F. A. Davis, president of the F. A. Davis Company, my publishers, and Dr. J. Madison Taylor, my associate in the editorial management of the "Monthly Cyclopædia of Practical Medicine." Several of the microphotographs presented in this volume were prepared by my son, Dr. Louis T. de M. Sajous, from slides. Some of these I owe to the kindness of Professors George A. Piersol and D. J. McCarthy, of the Medical Department of the University of Pennsylvania, to whom I wish to express my thanks.

C. E. DE M. SAJOUS.