Solids.	Grains.
Ferrous carbonate	0.55
Silica	7.42
Alumina	Traces.
Organic matter	2.60
Total	201.19
Free carbonic acid gas	265.76

In the writer's treatise on the "Mineral Waters of the United States" (1899) this water is classified as an alkaline carbonate. It is cool and sparkling and very grateful to the palate. The resort offers numerous advantages to the seeker after health and recreation. Fogs are rare in Lake County, and the air is uniformly dry and pure, resembling that of Nice in the south of France. The water is stated to be highly recuperative to persons suffering from portal congestion and chronic dysentery. It is further recommended in rheumatism, chronic Bright's disease, and chronic inflammatory states of the female generative organs. Facilities for bathing have been provided. *James K. Crook.*

ADDISON MINERAL SPRINGS.—Washington County, Maine.

Post-Office.—Addison.

Access.—Via steamer from Portland. Hotel and private families accommodate visitors.

This spring is located in a charming hilly section within one-quarter of a mile from an inlet of the Atlantic and about one hundred feet above the ocean level. It is about five feet in diameter and four feet in depth, and has a steady and rapid flow. The following analysis furnished to the writer by Mr. W. H. Nash, one of the owners, was made by Professor Hayes. The figures presumably have reference to grains per United States gallon:

Solids.	Grains.
Potassium sulphate	0.60
Sodium sulphate	0.27
Iron bicarbonate	1.65
Calcium sulphate	0.52
Silica and alumina	Traces.
Calcium bicarbonate	2.65
Magnesium bicarbonate	1.12
Sodium chloride	0.89
Sodium bicarbonate	0.44
Total	8.14

According to the classification adopted by the author, this water is properly termed a light alkaline chalybeate. It has been used with apparent benefit in acid dyspepsia, renal congestion, and other conditions in which a mild antacid diuretic is required. *James K. Crook.*

ADDISON SULPHUR SPRINGS.—Webster County, West Virginia.

Post-Office.—Addison.

Access.—Via West Virginia and Pittsburg Railroad to Cowen; thence by stage twelve or fifteen miles to springs. A railroad now being constructed from a point on the former line will soon extend directly to the springs. Hotels and boarding-houses.

The springs here include two natural fountains and one bored well. Dr. George B. Simpson, of the Webster Springs Sanitarium, in the neighborhood, supplies us with the following partial analysis. One United States gallon contains:

Solids.	Grains.
Calcium carbonate, Magnesium carbonate	13.17
Calcium sulphate, Magnesium sulphate	19.36
Sodium chloride	377.32
Iron oxide	Traces.
Volatile and organic matter	57.45
Total	467.30

We have classified this water as a muriated saline calcic (*vide* "Mineral Waters of the United States"). Mr. R. H. Townsend, of Addison, informs us that it is also heavily impregnated with sulphuretted hydrogen. It has a temperature of 57° F. It has a strong salty flavor, but most persons find it quite palatable.

The town of Addison is picturesquely located on the banks of the Elk River. The situation is about fourteen hundred feet above the sea level, and the surrounding country is of a mountainous character with a variety of pleasing scenery. The place has nine small hotels, but the accommodations are not sufficient to provide for the increasing tide of summer visitors. Statements appear to agree that the waters here possess value in disorders of the alimentary tract and liver. They are of undoubted benefit in cases of chronic constipation and abdominal venosity. *James K. Crook.*

ADDISON'S DISEASE (Bronzed Skin Disease; Melasma Suprarenale).—Of the above terms the first is to be preferred, for while the peculiar discoloration of the skin is not an invariable characteristic of the affection, the credit of Addison to the discovery of the disease called by his name has never been called in question.

Definition.—A disease characterized by progressive asthenia, digestive disorders, pain and tenderness chiefly seated in the epigastric, hypochondriac, and lumbar regions; and an abnormal pigmentation of the skin and mucous membranes.

Historical Notice.—The first case of Addison's disease on record is to be found in Lobstein's treatise, "De nervi sympathici humani fabrica et morbis," Paris, 1823, from the English translation of which, by the late Prof. Joseph Pancoast, I take the following extract: "I have myself observed the nerves forming the suprarenal plexus much thicker in disease, where the capsulæ renales, which were more than twice as large as usual, had degenerated into tuberculous substance." The patient was an unmarried woman, twenty-five years of age, who died in "convulsive spasms analogous to the epileptic. . . . Nothing unusual was discovered in the body of this woman but the aforesaid change in the suprarenal glands, and the enlargement of the nerves."

Notwithstanding the fact that there is no record of any darkening of the complexion, the above was undoubtedly a typical case of Addison's disease, in which, moreover, death by convulsions is not uncommon. The observation regarding the thickening of the nerves in this, the first recorded instance of the disease, is of remarkable interest. The second case was recorded in the "Halle Hospital Reports" by Dr. Schotte, in October, 1823, and is published in vol. vii. of the *Deutsches Archiv für klin. Med.*, by Risel, in the course of his article "Zur Pathologie des Morbus Addisonii." The third case came under the observation of Dr. Richard Bright, at Guy's Hospital, in July, 1829. It is contained in Dr. Bright's classical "Reports of Medical Cases," and also figures as Case V. in Addison's original memoir. The lesions of the capsules were characteristic; there was no other affection of any consequence, and for the first time in the history of this disease it was noted that the "complexion was very dark." A few other cases were reported before the year 1855, when Addison published his work "On the Constitutional and Local Effects of Disease of the Suprarenal Capsules," but it was reserved for his sagacity to detect the relation between the well-marked constitutional symptoms of the affection, the peculiar pigmentation of the skin, and the structural changes in the suprarenal capsules.

It is no disparagement to the memory of Addison to say that the general acknowledgment of his discovery was retarded by his including in his treatise cases which, at the present day, would be rejected from the category of Addison's disease. Of his 11 cases there are but 4 uncomplicated with other affections, 2 complicated; while of the remaining 5, 1 was a case of softening of the brain with advanced kidney disease and tuberculous deposits in various organs, among others in one suprarenal capsule, and the other 4 were cases of widespread carcinomatous deposit, the suprarenal capsules being more or less involved in each. Addison was evidently under the impression that the symptoms of the disease were due to the suppression of the unknown function of the adrenals, and that, therefore, any destructive lesion of these bodies was capable of causing them. This view of the pathogenesis of the affection has been called in question by distinguished pathologists, who have insisted on restricting the term Addison's disease to a tuberculous inflammation of the adrenals. The original view of Addison, however, is resuming its sway and bids fair ere long to be generally adopted. As will be seen later on, the most reasonable theory of the pathogenesis of the disease is that of adrenal inadequacy.

Etiology.—Age, sex, and occupation are prominent factors in the etiology of this disease. The lesion of the adrenals being, in the great majority of cases, tuberculous, it follows that the affection is most common during those decades in which tuberculous processes prevail—*i.e.*, between twenty and forty years of age. Exceptionally, the disease may manifest itself both in adolescence and in old age, and it may even be congenital. For example, Belyayeff has reported the case of an infant born with a dingy yellowish-gray skin who died at the age of eight weeks. At the autopsy both adrenals were found in a state of cystic degeneration. The disease is much more prevalent in males than in females, and especially so among the laboring classes. Of 183 undoubted cases tabulated by Greenhow, 119 were males and 64 females, and more than nine-tenths of the whole number were engaged in laborious manual work. Several cases have been associated with psoas or lumbar abscess, the adrenals becoming involved by extension of the inflammatory process. In others devoid of such spinal complication, the origin of the disease has been attributed by the patient to overexertion of the spinal muscles. Such was the fact in one of my own cases, the patient's first symptoms having been weakness and pain in the back immediately following the occupation of weeding her garden. In cases like those last referred to, it is probable that the lesion was well advanced at the time of the overexertion or traumatism, the latter merely serving to awaken dormant symptoms.

Symptomatology.—To quote the words of Addison: "The leading and characteristic features of the morbid state to which I would direct attention are—anæmia, general languor and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of color in the skin, occurring in connection with a diseased condition of the suprarenal capsules."

Taking these in order, the anæmia first claims attention. As is well known, it was while studying the disease which he termed idiopathic anæmia, now more generally known as pernicious anæmia, that Addison, as he expressed it, "stumbled upon" the discovery of the disease which bears his name. With his mind intent upon the disease which presents the profoundest grade of anæmia, it was natural that Addison should attribute the languor and debility of the bronzed skin disease to a similar state of the blood. The anæmia of that affection is, however, more apparent than real. In one of the most typical cases on record, described and pictured by Byrom Bramwell in his atlas of clinical medicine, the red corpuscles numbered 3,250,000, while the hæmoglobin was present "in at least the normal amount." In another case of the same distinguished clinician the red corpuscles numbered 3,500,000 per cubic millimetre, *i.e.*, 70 per cent. of the normal. These figures certainly do not represent a high grade of anæmia. According to Dr. Wilkes, to whose vigorous and loyal efforts the general recognition of Addison's disease is perhaps chiefly due (Rolleston), anæmia is not a feature of the disease. Under the microscope the red corpuscles are seen to be of normal size and shape, and to form rouleaux as in health, while the white cells may or may not be slightly in excess. In one or two cases free pigment granules are said to have been present, but the observation stands in urgent need of confirmation. Anæmia not being present in sufficient degree to account for the profound asthenia of Addison's disease, to what then is it due? As will be seen under the head of pathogenesis, it is most reasonably to be attributed to an irregular distribution of the blood, to its accumulation in the enormous district of the abdominal vessels.

The languor and debility or, in one word, the asthenia which, according to Addison and all subsequent observers, is a cardinal symptom of the disease, is also one of the earliest. In all histories of the disease the patient has been compelled to abandon his usual occupation by reason of muscular weakness, and when there is no complication with other wasting disease this prostration is unattended, at least in the early stage, with any marked diminution in the volume of the muscular and adipose tissues. The power of resistance to depressing agents is greatly reduced. Mental and bodily exertion which would be regarded by the healthy as trivial, is followed by exhaustion, and the use of purgatives is positively dangerous. As remarked by Bramwell, in more than one of the recorded cases death has resulted from an ordinary dose of a purgative drug.

With this asthenia there is enfeebled action of the heart, of which the apex beat is faint or imperceptible and the sounds weak and distant. The pulse presents varying features, but is always weak and compressible. It may be frequent or infrequent, full or small. Patients are liable to attacks of collapse induced by vomiting, purgation, or other depressing cause, or without apparent cause, which may be so severe as to resemble the collapse of cholera. Contrary to the usual frequency of the pulse in collapse, a remarkable diminution in the number of the heart beats has been observed in several cases (Risel mentions seven), and this without any disease of the brain or important cardiac disease. In a case reported by Cholmeley (*Medical Times and Gazette*, 1869, vol. ii., p. 219) in which death was preceded by profound collapse, dyspnœa, and convulsions, the pulse fell to 36 per minute.

Symptoms referable to disordered digestion are always more or less prominent and are of early appearance. Among them are marked anorexia, nausea and vomiting, constipation alternating with diarrhœa, and epigastric tenderness. Sometimes the nausea and vomiting occur in paroxysms without any apparent exciting cause, and on this account, as well as because of their severity, they have been compared to the gastric crises of locomotor ataxia. Epigastric tenderness was a prominent feature of two cases that came under my care at the Episcopal Hospital of Philadelphia. In the report of the first I noted that "at times there was great tenderness about the umbilical region, and on one occasion, after palpating the abdomen, the patient uttered loud cries for ten or fifteen minutes and seemed in great agony" (Trans. Path. Soc. Phila., vol. v.). In the other case, "the pain was latterly most severely felt in the left lumbar region, in which situation there was also a great degree of tenderness on pressure" (Trans. Path. Soc. Phila., vol. x.). In the first of these cases nothing was found at the necropsy to account for this remarkable tenderness; in the second, it might have been due to the great tumefaction of the lumbar glands.

The date of the appearance of the pathognomonic discoloration of the skin from which the disease derives one of its names is very variable. It may either precede or follow the constitutional symptoms, or the disease may terminate fatally without its manifestation. Greenhow has collected a number of cases illustrating the erratic appearance of this, the only pathognomonic feature of Addison's disease. In one of his cases the pigmentation of the skin is said to have been the sole symptom for eight years, at the end of which period the pigmentation deepened and the other well-known symptoms of Addison's disease were superadded. This case is the most remarkable on record in so far as the early appearance of bronzing is concerned, but it has been criticised by Bramwell, who has shown that the original pigmentation, limited to the forehead and parts adjacent, was probably due to a chronic peritonitis, of which the signs were found at the autopsy, and that the genuine melasma suprarenale dated from the period when the pigmentation was observed to deepen and become more general, and the constitutional symptoms to develop.

In connection with the statement above made, that the disease may terminate without cutaneous change, it

is important to observe that the pigmentation may be very limited in area, and so situated as to escape observation unless the entire surface of the body is minutely inspected. The most remarkable illustration of this important point is furnished by Bramwell. He had exhibited at his clinique in the Edinburgh Royal Infirmary, a patient whose chief symptoms were moderate anæmia (3,500,000 red corpuscles per cubic millimetre), emaciation and extreme prostration, and had confessed his inability to make a positive diagnosis. As the patient was walking away to put on his clothes, "and when a good light fell full on his back, I noticed," says Bramwell, "two or three brown discolorations over the spines of some of the dorsal vertebræ. It immediately flashed across my mind that the case was one of Addison's disease. I at once called the patient back and carefully examined the mucous membrane of the mouth. A small brown discoloration was seen to be present on the inner side of the left cheek, just opposite the angle of the mouth. The discoloration was quite characteristic, and I immediately committed myself to a positive opinion that the case was one of Addison's disease."

The abnormal surface pigmentation has its seat in the skin and in the mucous membrane of the buccal cavity, including that of the tongue; it has been said also to occur in the vagina and the conjunctiva. The pigment is deposited in the youngest layers of the rete Malpighii, in contact with the papillæ. It appears both as a diffuse coloration of the cells and also in the form of distinct granules in the cells, or free; in the latter case it is supposed to be left after the dissolution of the cells. It rarely appears in the corium, although sometimes branched pigmented connective-tissue cells are found. The parts of the external surface most deeply pigmented are those which, under normal circumstances, are the seat of oft-recurring hyperæmia, either from atmospheric influences or friction, such as the cheeks, neck, and backs of the hands. There is also a special tendency to the deposit of pigment in those parts where it is found normally in greater amount than elsewhere, such as the nipples, genital organs, and axillæ. In well-marked cases, it pervades the entire cutaneous surface, being deeper in the parts above mentioned, and may be deposited in the lunule of the nails and even in the teeth. The hair and the iris have been observed to grow darker with the progress of the disease. The tint of the discoloration varies in different cases, depending to some extent upon the normal complexion of the patient. It is most striking, because of its incongruity, when the patient is naturally fair, with light hair and blue eyes. The color of the most typical cases of the disease may be best imitated by staining the healthy skin with walnut juice. In chronic cases, the complexion may come to resemble that of a mulatto, as in the portrait illustrating Bramwell's classical monograph ("Atlas of Clinical Medicine," vol. i.) which has been copied far and wide. When the pigmentation is partial, as it is apt to be in its early stage, its outline is not sharply circumscribed, as in other pigmentary affections, but gradually fades into the surrounding integument. Upon the darker patches also are frequently seen black specks resembling moles or freckles. As above stated, the pigmentation is most pronounced in parts that have been subjected to any species of irritation, such as that of a blister, or that produced by the pressure of garters, waist-bands, or suspenders. A well-known illustration of this effect of cutaneous irritation is afforded by the case of a baker's boy whose shoulders were marked with dark stripes corresponding to the lines of pressure of straps from which his basket was suspended.

Pigmentation of the mucous membranes is at least equal in diagnostic value to that of the skin, although it is believed by most authorities to be rarer and to occur at a more advanced stage of the disease. It is most frequently observed in the line of closure of the lip, and upon the tongue, cheeks, and gums, and is accented by any cause of irritation, such as that of a carious, jagged tooth. When seated in the gums the discoloration has been mistaken for that of lead poisoning. It may be of a dingy brown hue or darker, as if caused by ink stains. It has also been compared to the stains produced by whortleberries and blackberries. In one of Bramwell's cases the pigment was accumulated in round, ball-like masses on the under surface of the tongue parallel with and apparently adherent to the lingual arteries.

The urine presents no characteristic changes. The most careful study of the urine in any single case was made by Dr. Thudicum, for sixty-five consecutive days, in a patient of Dr. Burdon Sanderson. Without complicating fever or diarrhœa, there was a great diminution in the daily amount of urine, it being reduced more than one-half; the specific gravity was 1.020 and upward, and the reaction acid. The most important result of these researches was the determination of the fact that the urinary pigments were much diminished. Thudicum's analyses, so far as the estimate of the urinary pigments is concerned, have been since confirmed by Drs. A. E. Garrod and Dixon Mann. Thudicum was apparently of the opinion that the diminution in the amount of the urinary pigments might bear a relation to the excess of pigment in the skin; but it is more reasonable to suppose that if disease of the adrenals caused an accumulation of soluble pigments in the blood, the coloring matters of the urine, supposing the kidneys to be healthy, would be present in excess.

The remaining symptoms of Addison's disease are either inconstant or negative, and, therefore, of secondary importance. Most of them are referable to the nervous system and are dependent upon a defective or irregular supply of blood. Among them may be mentioned insomnia and somnolence, headache, vertigo, tinnitus aurium, neuralgic pains which may be seated in the joints, muscular twitchings, and epileptiform convulsions. The latter, associated with delirium and coma, may be the immediate precursors of death.

The temperature throughout the disease presents nothing characteristic, being, in the absence of complications, normal or subnormal. The nutrition in the earlier stages may be well maintained, and in uncomplicated cases there may be little loss of fat throughout the entire course of the disease. When associated with phthisis, however, or other wasting disease, and even sometimes without such association, emaciation may become extreme.

Pathogenesis.—There are two principal theories of the pathogenesis or "pathological physiology" of Addison's disease: 1, The nervous theory; 2, the theory of adrenal inadequacy.

1. *Nervous Theory.*—According to this theory, "the symptoms of Addison's disease are not directly due to the destruction of the suprarenal bodies, but result from the derangements in the abdominal sympathetic (and perhaps other nervous structures) which the lesion of the suprarenal capsules produces." This theory has, to support it, facts derived both from anatomy and from physiology. In the great majority of cases the nerves and ganglia of the abdominal sympathetic are extensively involved in the tuberculous inflammation which destroys the adrenals, and it is only reasonable to suppose that such involvement must give rise to serious symptoms. In addition, it has been demonstrated by Alezais and Arnaud that upon, and in the substance of, the capsule of the adrenals there are numerous sympathetic ganglia. These they term the *pericapsular nervous ganglia*, and they hold that the peculiar and special lesion of Addison's disease "is their degeneration." They explain the well-known absence of symptoms of Addison's disease in many cases of cancerous disease of the adrenals by the fact that the malignant growth advances from within outward and is limited by the fibrous covering of the glands, whereas tubercles invade both gland and fibrous covering alike. Semmola, of Naples, pushes the nervous theory to the extreme of holding that the abdominal nerves and ganglia are primarily involved, and that the lesion of the adrenals is a trophic result of their functional disturbance.

Granting, as every one does, the common involvement of the abdominal nerves and ganglia, and especially that

of the *pericapsular ganglia*, it remains to be considered whether the results of experiments upon the abdominal sympathetic throw any light upon the pathogenesis of Addison's disease.

Irritation of a sensory nerve produces vasomotor paralysis in the irritated region, and the well-known experiments of Goltz ("*Klopfversuch*") have shown that irritation of the intestines produces complete vasomotor paralysis of their blood-vessels, causing thereby so great an accumulation of blood that the animal shows symptoms of syncope, the same as if it had been bled copiously.

The irritation of the numerous nerves and ganglia of the adrenals produced by inflammation with new formation of tissue and subsequent softening, such as exists in Addison's disease, is transmitted to the semilunar ganglion and solar plexus from the beginning of the deposit in the adrenals, and, later, by extension of the inflammatory process to these nerve centres. By this means a vasomotor paralysis of the intestinal vessels is produced, as in the experiments of Goltz, except that, unlike in the latter case, it is constant. This continual hyperæmia of the intestinal vessels leads to enlargement of the solitary glands and Peyer's patches, so constantly found in Addison's disease, and occasionally to catarrh and ulceration of the stomach and intestinal mucous membrane. It accounts for the dark color of the liver, spleen, pancreas, and kidneys so often observed, as well as for the brownish hue of the peritoneum noticed in a few instances. Indirectly, it explains the anæmic and dry condition of other parts of the body, and directly accounts for the great muscular weakness, syncope, gastro-intestinal disturbance, dyspnœa on slight exertion, and small radial pulse. These symptoms have been attributed to a high grade of anæmia, such as exists in pernicious anæmia; and this is due to the fact that many of the symptoms in the two affections are identical. Repeated examinations of the blood have, however, demonstrated that the reduction in the number of the red corpuscles in Addison's disease is trivial compared with that found in pernicious anæmia. The symptoms resembling those of pernicious anæmia—such as dyspnœa on slight exertion, syncope on assuming the upright posture, rapid, small, and feeble pulse—are attributable to an insufficient supply of blood, albeit of fair quality, to the supradiaphragmatic portion of the trunk.

From the foregoing, it is manifest that there are well-established facts, both anatomical and physiological, in support of the nervous theory of Addison's disease. This is the theory adopted by Bramwell, although he qualifies his adherence to it by the statement that it is "perhaps possible that some of the symptoms of Addison's disease may be the direct result of abolition of the [glandular] function of the suprarenal capsules."

Rolleston (*British Medical Journal*, April 6, 1895) discards the nervous theory rather summarily, and chiefly, as it seems to the writer, on the ground that the "sympathetic in the neighborhood of the suprarenal bodies is not constantly altered." It must be recalled, however, that Alezais and Arnaud discuss this contingency, and claim that Addison's disease is "accompanied with alterations in the pericapsular sympathetic nervous system and with complete integrity of the rest of the solar plexus and its ganglia."

2. *Theory of Adrenal Inadequacy.*—The arguments in support of this theory are derived from analogy, anatomy, therapeutics, and experimental pathology.

The structure of the adrenals is distinctly glandular. In the vast majority of cases, the symptoms of Addison's disease are associated with destruction of these glands. In the rare cases in which they are destroyed by disease without concomitant symptoms of morbus Addisonii, the absence of the latter may be due to accessory suprarenal bodies or to suprarenal "rests." The former, according to Rolleston, are "very commonly present in the connective tissue in the immediate neighborhood of the two organs"; the latter, the so-called "suprarenal rests," are found "embedded in the kidney or liver." The analogy with myxœdema is thus seen to be very close, and, to make it complete, it need only be added that the life of an animal whose adrenals have been removed may be prolonged by embedding beneath its skin a healthy adrenal or administering subcutaneously an adrenal extract.

The experiments upon the function of the adrenals which seem to the writer to be the most free from criticism are those of Abelous and Langlois (*Archives de physiologie*, tome iv., 1892). These observers found: (1) that the total destruction of both adrenals in frogs was invariably followed, sooner or later, by death, the time of which depended upon various factors. Frogs in a state of hibernation survived the operation for twelve or thirteen days, while in the summer the animals never lived longer than forty-eight hours. If the animal was irritated so as to excite active muscular movements, it perished sooner than if it were allowed to remain quiescent. In other words, the more active the nutritive changes, the sooner the animal died—a fact in accordance with the longer survival of hibernating animals as compared with those operated on during the summer.

(2) The destruction of one adrenal did not cause death or any abnormal manifestation (six animals operated on).

(3) If one adrenal is destroyed and a large portion of the other, the animal may or may not die. A considerable portion (*un fragment notable*) of one adrenal must be left in order to insure the survival of the animal.

(4) The insertion beneath the skin (in the dorsal lymph sac) of the adrenals taken from a sound frog prolongs the life of a frog from which both adrenals have been removed.

(5) The injection (subcutaneous) of adrenal extract into frogs from which the adrenals have been removed prolongs their lives but a short time—not more than twenty-four hours.

(6) The injection (intravenous or subcutaneous) of blood from a frog about to die from the effects of loss of adrenals into a frog from which the adrenals have just been removed, causes rapid paralysis and death. The same injection into a normal frog produces very slight and transitory disturbances.

In none of their experiments did Abelous and Langlois observe any anomalous pigmentation.

They conclude from their experiments, of which the above is but an abstract: (*a*) that the death of frogs after removal of their adrenals is due to the accumulation in the blood of one or more toxic substances; (*b*) that this substance, or these substances, produces an effect resembling that of curare, acting chiefly upon the terminations of the motor nerves and slightly also upon the muscles. The rôle of the adrenals, in their opinion, is to destroy this poison by an internal secretion which they elaborate.

So much for the theory of adrenal inadequacy, which is the one adopted by Rolleston, who concludes his elaborate and masterly discussion of the pathogenesis of Addison's disease (Goulstonian lectures, *British Medical Journal*, 1895) with the statement that the affection "is due to an inadequate supply of suprarenal secretion. Whether the deficiency in this internal secretion leads to a toxic condition of the blood, or to a general atony and apathy, is a question which must remain open."

More careful observation is needed to determine whether the symptoms of those cases of Addison's disease in which the sympathetic nerves and ganglia are implicated, are different from those in which they are not. Judging from the well-known results of physiological experiment, it would seem reasonable to expect a greater degree of asthenia and a greater tendency to syncope in cases of sympathetic involvement, and, on the other hand, to expect a predominance of more purely toxic symptoms in those cases (the type of which is simple atrophy of the adrenals) in which the lesion is limited to the capsules. The supreme judge of this question, as of all questions of pathogenesis, is the clinician, and with greater opportunities for observation, the expectation of its solution is not unreasonable.

Diagnosis.—When the disease is primary, the constitutional symptoms well marked, and the discoloration of

skin and mucous membranes present, the diagnosis presents little or no difficulty to one who has previously studied a single case of the disease. On the other hand, when the constitutional symptoms are well pronounced in a primary case, and the bronzing of skin is not yet developed, the diagnosis is to be made only, if at all, by the exclusion of other wasting diseases, especially cancer of abdominal organs and progressive pernicious anæmia. Many years ago there came under my care at the Episcopal Hospital of Philadelphia a case of lumbar abscess with several open sinuses leading to carious vertebræ. The general surface of the body was of a dark dingy hue, and the orifice of each sinus was surrounded by a broad, deeply pigmented ring. The patient had been previously at another institution, where secondary disease of the adrenals had been suspected. The autopsy showed these bodies to be perfectly healthy and the kidneys to be involved in extensive amyloid degeneration. A dingy discoloration of the skin is not uncommon in amyloid disease of the kidney, as first pointed out by Grainger Stewart.

The discoloration of skin, although not the most essential characteristic of the disease, is justly regarded as its most important diagnostic feature. It is to be distinguished from melasma gravidarum, pityriasis versicolor, lichen, and pigmentary syphilides, and this is readily done by any one familiar with these affections. The melanoderma of phthisical patients presents more serious difficulty. Although the latter is often confined to the face and does not invade the mucous membrane of the buccal cavity, the difficulty is a real one, and is augmented by the fact that pulmonary tuberculosis is the most frequent complication of Addison's disease. The seat of the melasma suprarenale, or its greater intensity, upon the face and neck, the dorsum of the hands, areola of the nipple and about the umbilicus, in the axilla, groin, and upon the genitals, is characteristic. Other diagnostic features of the pigmentation have been described above under the head of Symptoms. A discoloration of the skin liable to be confounded by the inexperienced with that of Addison's disease is sometimes seen in badly nourished paupers of dirty habits, whose skin is the abode of vermin. This pigmentation shows itself in the form of patches separated by healthy skin; the epidermis is often roughened, and the discoloration more marked upon the trunk than on the face and hands. The skin is also often marked with scratches, the result of the intense itching. Under the microscope, the particles of pigment in this affection are found in all the layers of the epidermis, instead of being limited, as in Addison's disease, to the deeper layers of the rete Malpighii. The pigmentation of chronic malarial poisoning is distinguished from that of Addison's disease not only by its distribution, but by the history of the case and the frequent presence of splenic enlargement; chronic icterus, with which Addison's disease was formerly confounded, is distinguished by the presence of pigment in the ocular conjunctiva and in the urine.

Other discolorations of the skin simulating closely the pigmentation of Addison's disease are mentioned by systematic writers, but are so rare as to be in themselves pathological curiosities. Among them may be mentioned a diffuse pigmentation associated with chronic scurvy (Bramwell), and a few other cases of melasma occurring without obvious cause. According to the author just cited, there are certain forms of pigmentation of the skin associated with chronic peritonitis, or malignant disease of the abdomen or pelvis, which it is impossible to distinguish from Addison's disease. This fact, though discomfiting to the clinician, is of great interest to the pathologist, as tending to prove that the most characteristic symptom of the affection, the melasma suprarenale, is to be attributed rather to the implication of the abdominal sympathetic than to that of the adrenals.

Prognosis.—The prognosis is in the highest degree unfavorable, although recoveries of cases presenting every sign and symptom of the affection have been reported by the most competent observers. Among these may be mentioned Sir William Gull and Dr. Finney. In making predictions as to the duration of life, the remittent character of the disease should be borne in mind. A case seen during a period of exacerbation may lead to the prognosis of a speedily fatal result, but the worst symptoms may disappear and be followed by a prolonged period of remission. The average duration of the life of hospital patients who, as a rule, do not apply for treatment until forced to acknowledge the fact of their illness, has been estimated at two years. Sudden death without preceding exacerbation is sometimes observed, the fatal result being apparently due to syncope.

Treatment.—At the present time, there may be said to be a specific treatment of Addison's disease—that with adrenal extract. This fact, however, in no way diminishes the importance of general therapeutic measures, of which the most important are the following: The cessation of work is the first thing to be insisted upon in the way of treatment, and during the exacerbations strict confinement to bed. An immediate mitigation of the symptoms has often followed the admission to hospital of a patient who, up to that time, had been endeavoring to resist the gradually increasing asthenia. A moderate amount of stimulants is generally well borne, but cod-liver oil, which might seem appropriate on account of the tuberculous nature of most cases of the disease, is, as a rule, not tolerated. Remedies to allay irritability of the stomach are frequently indicated, such as ice, lime water, carbonic acid water with brandy, bismuth, creosote, hydrocyanic acid, and small doses of opium. Massage and faradization are well worthy of a trial in order to derive the blood from the abdominal vessels. Iron and arsenic should be employed tentatively and will be generally found useful, and the same is true of nux vomica and its derivatives. Cathartics are to be avoided, as profound depression has often followed their employment in this disease. When constipation is troublesome it should be relieved by enemata and suppositories. The diet should be simple but nourishing, consisting of soups, milk, eggs, meat jellies, koumyss, and the like.

Treatment with Adrenal Extract.—The success that has attended the use of adrenal extract is such as to make it imperative in all cases of Addison's disease. This is not a mere *obiter dictum*, but is the result of a careful study of many of the reports upon the subject. A few examples will suffice to show the kind of evidence on which the administration of the adrenal extract is based.

Osler (*International Medical Magazine*, February, 1896) reports a case in which there was marked improvement under the use of the extract, attended with considerable gain in weight and restoration of general vigor. The pigmentation, however, which was of advanced grade, had not diminished except on the palate. A case is reported by Suckling (*British Medical Journal*, May 28, 1898) in which the symptoms and signs were well pronounced except pigmentation of mucous membranes, of which there is no mention. Tablets of suprarenal extract (āā gr. v.) were given to the extent of from twenty to thirty-five daily. In the course of a year recovery was complete with disappearance of melanodermic and leucodermic patches. Kinnicutt has tabulated 48 cases (*American Journal of the Medical Sciences*, July, 1897) treated with adrenal preparations. "Six patients are reported as cured or practically well, 22 improved, 18 unimproved, and in 2 instances an aggravation of the symptoms is stated to have occurred during treatment." In the second class of cases, those in which improvement took place, the improvement was but temporary; but this was as much as could be expected, since in many the disease of the adrenals was associated with grave tuberculous lesions in other parts of the body.

On the theory that Addison's disease is chiefly due to suppressed function of the adrenals, the use of adrenal extract would find its most successful employment in those cases in which the lesion consists of simple atrophy or fibroid degeneration. *Frederick P. Henry.*

ADENITIS. See *Lymphatic Glands, Diseases of.*

EXPLANATION OF
PLATE VI.