to magnetic or electric disturbance, but also it may be owing to the fact that an intense aurora is not followed by a storm, indeed is almost sure to be, if we may trust the recent observations of Lieut. Weyprecht of the Austrian Polar Expedition; also it is a common belief among our northern Indian tribes. The pain, then, which followed the northern light may be merely an ordinary storm-pain; but the question deserves a more exact answer.

There seems, then, to be every reason to believe that the popular view which relates some pain fits to storms has a distinct foundation, and, as we have seen, it has stood the test in this single case of a long and patient scientific study. At the same time we have failed to detect the single element of mischief, and are thus far driven to believe that it is the combination of atmospheric conditions which starts the pain into being.

A still more valuable and novel conclusion has arisen out of our study. Every storm, as it sweeps across the continent, consists of a vast rain area, at the centre of which is a moving space of greatest barometric depression, known as the storm-centre, along which the storm moves like a bead on a thread. The rain usually precedes this by 550 to 600 miles, but before and around the rain lies a belt, which may be called the neuralgic margin of the storm, and which precedes the rain about 150 miles. This fact is very deceptive, because the sufferer may be on the far edge of the storm-basin of barometric depression, and seeing nothing of the rain, yet have pain due to the storm. (Diagram No. 11.)

It is somewhat interesting to figure to one's self thus—a moving area of rain girdled by a neuralgic belt 150 miles wide, within which, as it sweeps along in advance of the storm, prevail in the hurt and maimed limbs of men, and in tender nerves and rheumatic joints, renewed torments called into existence by the stir and perturbation of the elements.

I give (Fig. 11) a diagram of one storm with the theoretical rain area as founded on Prof. Loomis's observations, and its neuralgic belt as founded on our own observations.

ART. II.—*Addison's Disease, and its Relations with Anæmatosis (Essential Anæmia).* By WILLIAM PEPPER, A.M., M.D., Professor of Clinical Medicine in the University of Pennsylvania.

IN the number of this Journal for October, 1875, I gave some account of a rare form of disease, under the name of "progressive pernicious anæmia." I endeavoured to show that this affection, which has lately been made the subject of numerous interesting memoirs, is identical with the "idiopathic," or "essential" anæmia of Addison. Attention was also drawn to the

remarkable resemblance between the chief symptoms of progressive pernicious anæmia, and of some forms of leukæmia and pseudo-leukæmia; and also to the fact, as appeared from one of the cases reported at length (Case No. III. p. 325), that there is a lesion of the marrow of the bones in the former disease similar to that which has now been repeatedly found in the latter affections. I ventured, therefore, to suggest the view that the progressive pernicious anæmia of recent writers may be, in some instances, at least, the medullary form of pseudo-leukæmia; although of course it is necessary that a careful examination of the marrow in a number of such cases should confirm or refute this opinion before it can be disposed of definitely. Finally, I called attention to the fact that the various accepted forms of leukæmia and pseudo-leukæmia (including progressive pernicious anæmia) are so much alike that they can only be distinguished by the varying degrees of increase of the white corpuscles of the blood, and the preponderance of the lesions of the spleen, the lymphatic glands, or the marrow; and that they are all associated with lesions of the blood-making tissues, and are especially characterized by a profound alteration of the blood-making function (hæmatosis). Consequently I suggested the name of anæmatosis (α privative; αιματοσις, elaboration of blood), signifying impairment, defect, or *disease of the blood-making function*, for this entire class of affections, specifying their various forms by the terms *splenic*, *lymphatic*, and *medullary*.

I have recapitulated these points, in order to bring the consideration of another interesting affection, Addison's disease, more directly into connection with the study of these cachexiæ. The affection known as Addison's disease is one about whose nature and pathology many different views have been, and still are held. Besides the above name, given to it in honour of the first describer, it has been called the bronze disease, suprarenal cachexia, melanopathia, asthénie sur-rénale, and melanodermie asthénique. These and other names, of themselves indicate our ignorance of the true nature of this disease, and the attempt to designate it merely by naming some of its chief symptoms.

It is undoubtedly a rare disease in America, and but few complete cases have been placed on record in our journals. In the number of this Journal for January of the present year (p. 75), I have published a detailed account of a typical case of Addison's disease, to which reference will occasionally be made in this article. I shall refer to it as the case of Mr. C. L. So soon as I met with cases of so-called progressive pernicious anæmia, or anæmatosis, I was struck by the numerous analogies presented by their symptoms and course with those of Addison's disease; and in consequence, I awaited anxiously the publication of reports of cases of the latter affection, in which microscopical examination of the marrow of the bones should have been made. But as no such examinations have yet, to my knowledge, been made, the following cases and remarks, in connection with the

case above referred to, are offered as a contribution to the clinical study of this interesting question. No attempt will be made to present a complete historical sketch of Addison's disease, and it will be necessary to avoid even a passing allusion to most of the interesting memoirs lately published on this subject. Nor will it be possible in the limits assigned to this article to present all the arguments for and against the various theories which have been advanced, as to the nature and pathology of Addison's disease. The object is rather to present a broad sketch of the leading characteristics of the affection, and then to bring them into comparison with the symptoms of certain other conditions. In discussing questions of so much difficulty as that upon which we are now writing, it is peculiarly important to avoid preconceived opinions, or hasty conclusions; and, in offering some considerations which appear to favour a view of Addison's disease different from that which is generally adopted, the hope is merely entertained that they will seem of sufficient value to receive attention from future investigators of these important subjects.

It would occupy too much space to quote in full the classical description which Addison first gave in 1855, and to which scarce anything has been added by subsequent writers; but the following brief summary, which he gives, of the leading and characteristic features[1]—"anæmia, general langour and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of colour in the skin," will show the identity of the case of Mr. C. L. with the morbid state which Addison was the first to connect with diseases of the supra-renal capsules.

As, however, a certain degree of irregularity is frequently to be observed in the development of the symptoms or in the course of the affection, it is necessary to discuss its principal features more in detail.

Mode of Origin. Early Symptoms.—As a general rule in this, as in other cachectic conditions, the appearance of the symptoms is so insidious that the patient can rarely refer to any particular date or occurrence as marking the beginning of the disease. Occasionally, however, it seems to be more abrupt in its development, and to run a more acute course. In these cases, which occur especially in young persons, the lesions generally show that latent disease of the supra-renal capsules has been progressing for an uncertain length of time, and that the constitutional symptoms have been quite suddenly developed in their full form. In most cases, the earliest symptoms complained of by the patient are slowly-increasing debility and loss of energy. It may be that dull, deep-seated pain in the loins has been noticed for some time previously; thus Mr. C. L. had observed, for a considerable time before the development of the characteristic symptoms, that

[1] On the Constitutional and Local Effects of Disease of the Supra-renal Capsules; Syd. Soc. Ed. of his works, p. 211.

certain exertions, such as bending or lifting, caused dull pain in the loins. Disturbances of digestion, capricious appetite, nausea, occasional vomiting, may also appear early. The discoloration of the skin, which justly attracts so much attention, very rarely appears as the initial symptom. Among the more rare symptoms, which have been occasionally noted as preceding or accompanying the development of the disease, are transient attacks of jaundice, rheumatoid pains, excessive urination (polyuria), diarrhœa with colourless stools, and marked pulsation of the abdominal aorta, simulating aneurism. After the symptoms are well established, we may note with care the differences which exist in individual cases in regard to the following features :—

Nervous Symptoms.—The muscular debility, to which reference has been already made, ranks first among these, and merits careful study. Frequently the very earliest symptom noticed, it continues throughout the case to be the most remarkable. At first, the patient merely observes that he tires in the performance of his day's work more readily than usual. The debility increases with greater or less rapidity until the patient is barely able to leave his bed, or even to sit up without urgent symptoms of exhaustion. In some cases the disease lasts between two and seven years before it reaches this extreme degree; in others, it is attained in the course of as many months. In some instances, so rapid and sudden is the loss of strength that the disease may be mistaken for an attack of typhoid fever; and it will be observed that in the case of Mr. C. L. this mistake was made by the family of the patient. Scarcely ever does it progress continuously; but, as will be observed in a very marked manner in the case which furnishes the basis of this article, from time to time there is a rapid and marked return of strength, so that, for example, a patient who has been barely able to sit up in bed, will soon be strong enough to walk about or even to do light work. This improvement is very deceptive, and as in some cases it lasts a considerable time, it has led to some confusion with regard to the beneficial effects of certain modes of treatment. In almost, if not actually in every case, however, this improvement is but delusive; and, after lasting an uncertain period, is rudely interrupted by some apparently causeless attack which rapidly reduces the patient's strength to a point even lower than at any previous time. When this symptom has become well developed, there may be, even during entire quiet, a profound sense of exhaustion; or, as was noted in Mr. L.'s case (p. 78), there may be an utter loss of desire for exertion or even for movement, a profound lassitude which leads the patient to repose contentedly in perfect quiet day after day. The power of clasping with the hand may seem to be fair, and while the patient is lying down, he may appear to still have considerable strength, but the act of rising to the feet, or even of sitting up, induces rapid and extreme exhaustion. In the case here referred to, the patient, after his debility became advanced, preferred

making no effort to sit up, and when obliged to leave bed in order that the clothes might be changed, would slip down in a minute from the chair where he was placed on to the floor, where he would lie at full length.

It appears to me that the characters of this excessive debility are best explained by the view that it is dependent upon an anæmic state of the nerve centres, associated with great enfeeblement of the heart's action.

Months before the fatal result of the case, and when perhaps the patient will still rally several times and become able to make considerable exertion, we meet with a degree of muscular weakness scarcely equalled even in the last stages of any chronic disease. It is more closely approached by the debility described in the cases of "progressive pernicious anæmia" reported in the number of this Journal for October, 1875, than by other condition I know of. In Addison's disease, moreover, as will be hereafter seen, it is probable that (in many cases at least) there is a state of irritation of the abdominal ganglia of the sympathetic or of other nerves which aids, by inhibitory action on the spinal cord, in the production of such intense asthenia.

In addition, it will be noted that Mr. L. complained of a peculiar sense of straining in the joints or muscles when he made any sudden movement.

Other nervous symptoms are occasionally met with, but cannot be ranked among the characteristic features of the disease. Among these may be mentioned convulsions, which sometimes occur shortly before death, or more rarely precede the development of the disease. In the few instances where the latter has occurred, it is difficult to determine what, if any, is the connection.

In other cases numbness or partial anæsthesia, tremors or muscular twitchings have been noticed, but none of these occur with sufficient frequency to make them rank among the symptoms of the disease. They probably depend upon some special minute lesion of the nervous system. The giddiness which is occasionally noticed, is probably dependent upon the anæmia and the feeble condition of the systemic circulation.

Digestive Symptoms.—In nearly all cases there are marked disturbances of digestion present. The appetite remains fair for a time, but then grows capricious and irregular or fails in a marked degree. On page 80 (report of Mr. C. L.'s case) will be found a detailed account of some of its peculiarities. Nausea is often present, and in some cases the presence of food in the stomach causes marked distress. Vomiting is scarcely ever absent throughout the course of the disease, but, like the other symptoms, is subject to marked alternations. At times, during the temporary spells of improvement already described, the appetite may become quite good and neither nausea nor vomiting occur. But in a variable time, often without any assignable cause or from some trifling over-exertion or indiscretion in

diet, a severe attack will occur attended with anorexia, nausea and frequent vomiting.

The peculiar irritability of the pharynx and œsophagus described on p. 80 is an unusual symptom.

The condition of the bowels is equally variable. In some cases, diarrhœa, due to follicular enteritis, appears among the earliest symptoms; and has even been ascribed as an occasional cause for the subsequent development of Addison's disease. It is true that, in many instances, enlargement of the solitary follicles of the intestine is found, but as a rule the condition of the bowels is one of moderate constipation, with occasional alternations of diarrhœa with thin, serous stools. In Mr. L.'s case these spells of diarrhœa were attended with cutting abdominal pain and great nervous restlessness, agitation, and prostration.

The abdomen is usually rather retracted; and may be indolent throughout the case, while, on the other hand, tenderness of quite marked character may be present. In Mr. L.'s case this was found at the epigastrium, and was associated with unusually great reflex irritability of the abdominal muscles. There is no alteration in the size of the liver, but a slight degree of enlargement of the spleen is generally present.

The *urine* presents no characteristic changes. It has been found to be excessive in some cases, but usually it continues normal or even reduced in quantity. It is reported to be frequently of low specific gravity and deficient in solid ingredients. It never contains albumen unless there be coincident organic disease of the kidneys.

Respiratory Symptoms.—In uncomplicated cases of Addison's disease the only symptom connected with the lungs is dyspnœa on exertion, resulting from the conjoined effect of anæmia and debility. This is at least true of the early period of the disease, though later it is quite common to note the appearance of cough with slight muco-purulent sputa, and the physical signs at the apex of one or both lungs of tuberculous(?) disease, of limited extent. In the case here reported, no dyspnœa was noticed until towards the close, when debility was extreme and a small degree of pulmonary disease had occurred.

The *circulatory system* furnishes much more important symptoms. The heart's action is feeble, and the pulse is very small and weak. During quiet it may rise but very little above the usual rate; but even slight exertion accelerates it and is apt to bring on palpitation. During the paroxysmal exacerbations of the disease, the pulse is usually much disturbed, becoming more rapid, 100 to 120, and at the same time extremely small, thread-like, and feeble. In the last stages of the disease the pulse is apt to be accelerated, but in some cases it is unusually slow, as in one reported by Dr. H. Thompson, where it varied from 52 to 60 within a fortnight of the death of the patient.

Cardiac or *vascular murmurs* of hæmic origin, connected with the

altered condition of the blood, are occasionally detected, but by no means so frequently as might be expected. In neither of the cases I have had the opportunity of carefully studying, were such murmurs present.

Abnormal pulsation of the aorta is present in a large proportion of cases; and its detection is rendered more easy by the retraction of the abdominal walls which often exists. In some cases there has been an apparent dilatation of the vessel (Gerhardt), but, as is well known, this is not an unusual sensation in connection with excessive local pulsation of large arteries.

The *state of the blood* is one of the most important conditions in this disease, and bears directly upon some of the most interesting questions as to its pathology and the nature of the symptoms. Unfortunately, however, the number of careful examinations which have been made is so small, and the results are so indefinite and even contradictory, as to render it very difficult to form a correct opinion as to the condition of this fluid.

Partly in consequence of this we find one of the most able and zealous investigators of the nature and symptoms of Addison's disease, Dr. Greenhow,[1] in his latest publication on the subject, expressing his opinion that the composition of the blood does not undergo any important alteration in uncomplicated cases of this affection. On the other hand, the existence and extreme degree of the anæmia occupied a prominent place in the group of symptoms which Dr. Addison established as characteristic of the disease he first described. It is true that accounts of the condition of the blood very rarely describe it as presenting the thin, watery consistence and light colour so characteristic of anæmia. On the contrary, in a fair proportion of the cases where its condition is referred to at all, the colour and consistency are spoken of as normal, and in one case reported by Greenhow the blood is even described as thicker than natural, with an excess of red globules. Still it must be remembered that these are but superficial means of judging of the blood. I have, in a former article already referred to (in the number of this Journal for October, 1875), spoken of the vague meaning of the term anæmia, and of its utter insufficiency to express all of the important forms of defective constitution of the blood.

It seems to me evident that, though the blood may not present the characters of ordinary anæmia, there must be grave interference with the healthy state of this fluid. In the first place, it appears undoubted that a great reduction in the mass of the blood usually takes place. This is suggested by the appearance of those parts of the surface which are free from the peculiar discoloration which is so characteristic of the disease. Thus the conjunctivæ are pearly white, and the matrix of the nails appears peculiarly white, far more so than could be explained merely by contrast with the surrounding discoloured skin. The marked degree in which this

[1] Med. Times and Gaz., June 12, 1875, p. 630.

appearance exists is shown by the frequency with which such terms as anæmic or chlorotic are used to describe the condition of the patient. Many of the symptoms, as will be further pointed out, seem to indicate and depend upon a deficiency of blood in the vessels. Finally, at the post-mortem examination, there is extremely little blood in the vessels or in the viscera with the exception of the lower part of the lungs and the right cavities of the heart. In the case of Mr. C. L. this decrease in the amount of blood in the vessels and tissues was very marked.

Again, in a great majority of those cases in which microscopic examination of the blood has been made, an excess of white corpuscles has been noted; according to Hayden, it has been detected in every instance where careful examination has been made. In some instances this excess is slight, in others marked; in a case reported by Severini (*Schmidt's Jahrb.* cxlii. p. 111), the white and red corpuscles seemed about equal in number. It has not been determined in what proportion of cases this increase takes place, nor whether it depends upon an actual increase in the number of white corpuscles, or is merely relative and dependent upon a great reduction in the number of the red globules. Possibly here, as is the case in other forms of disease of the blood-making function, both of these conditions may be present; in one set of cases, the element of increased formation of white corpuscles being present, while in another set there is only an apparent increase, due to the deficiency of red globules, which would seem to be more constant. It must not be forgotten that the dark colour of the blood may in part be due to some alteration in character or increase in quantity of its colouring matter.

The *fibrin* of the blood is apparently not greatly decreased, since it is usual to find small clots in the cavities of the heart. In Mr. L.'s case there were such clots, and on expressing the serum which they contained, they presented a peculiar and unusual whiteness.

I know of no instance where a careful analysis of the blood in Addison's disease has been made, but, on the whole, it seems clear to me that there is in this affection a profound interference with the elaboration of the blood, marked by decrease in the amount of blood and of the red globules, with or without actual increase in the proportion of the white corpuscles. If this be so, it would justify the use of the term "*anæmatosis*," which I have suggested for the condition present in the group of diseases comprising leukæmia, pseudo-leukæmia and progressive pernicious anæmia, and would indicate the possibility of further analogies between them and Addison's disease. I shall have occasion to return later to this interesting question.

Hemorrhages.—Closely connected with the question of the condition of the blood is that of the liability to hemorrhages which, in Addison's disease, are far from being common. It will be seen, hereafter, that minute extravasations of blood may be found after death in various parts, but

during life the liability to hemorrhages is much less than in some apparently allied diseases, such as progressive pernicious anæmia.

Emaciation usually exists to a slight or moderate degree; but, unless there is some complication of a serious character, there is no such wasting present as is seen in many chronic diseases.

Temperature.—Among the symptoms recorded in some cases, especially in the early stages of those which run a comparatively rapid course (as in a case by Heckford, *Lancet*, March, 1867), are slight rigors with very moderate febrile reaction (100° to 100.5° F.); and occasionally there is slight, irregular fever at intervals during the course of the case. But such cases are, perhaps, the exceptions, and it would seem to be the rule for the temperature to remain normal, or even to show a tendency to fall below the natural standard. In Mr. L.'s case it was never observed above 100° F.; more frequently it varied from 98.5° in the morning to 99.5° in the evening. But at times, when the exacerbations occurred, which we have already described, although the temperature of the trunk did not vary much, the extremities grew very cool, even so far up as the thighs and elbows. The difficulty in maintaining the bodily warmth is shown by this tendency to coolness of the extremities, and, in a very marked manner, by the severe effects of exposure to even moderate cold.

Discoloration of the Skin.—I have postponed until the last the discussion of this symptom, which has erroneously been regarded as the most important and characteristic feature of the disease. It is to this error that very much of the confusion which still surrounds the subject of Addison's disease is due. It is essential, then, that we should endeavour to obtain clear and definite ideas of the character and value of this symptom. In the first place, it is evident from a study of the recorded cases, that the discoloration of the skin is not among the earliest symptoms of the disease, but that the disease of the supra-renal capsules, with the consequent debility and changes in the blood, has often been progressing for an indefinite time—months, or even a year or two—before discoloration of the skin makes its appearance.

Again, it appears that it cannot be regarded as an *essential* symptom, and that there is no definite relation between the degree of discoloration and the development of the general symptoms and the extent of the lesion of the capsules. As a general rule, it is most intense in cases which run a very slow and chronic course. On the other hand, in some cases where the characteristic symptoms were very marked and severe, and the characteristic lesion of the capsules present, it is stated that there was no discoloration at all; and although it is possible that in some of these a slight shade of discoloration may have existed and been overlooked, it appears certain that in others (cases by J. B. S. Jackson, Gull, Niemeyer) it was entirely wanting.

It is probable that the explanation of these instances is that death has

been induced by exceptional individual weakness or unusually severe functional disturbances before time was given for any marked accumulation of pigment.

It is further to be remembered that discoloration of the skin (not always to be distinguished, even by the most careful study, from that which attends Addison's disease of the supra-renal capsules) may be produced by various causes, such as uterine disease, malarial fever, hepatic disease, or cancerous or tuberculous peritonitis. (See Case I.)

Finally, it has been clearly shown that various diseases of the supra-renal capsules, such as cancer, tubercle, or hemorrhage, may occur without the production either of discoloration of the skin or of the characteristic general symptoms; and that it is only one form of disease, viz., chronic inflammation with cheesy degeneration and sclerosis of the capsules, that induces the symptoms recognized by Dr. Addison. (See Case II.)

It is evident, therefore, that it is only by studying the discoloration of the skin in connection with the general symptoms that we can, in any case, assign to it its proper significance.

The discoloration itself is also deserving of close study, both in regard to its character, its distribution, and its progress and mode of development.

In typical cases the skin assumes a peculiar yellowish-brown colour, which can be best described by saying that the patient comes to look closely like a mulatto. Sometimes the brown colour predominates and the surface assumes a light mahogany tint, or as though the skin had been washed with walnut-juice. The term *bronzing* of the skin, which has been very frequently used, serves to describe the general character of the discoloration very well. Niemeyer speaks of the skin sometimes presenting a pure gray colour, inclining to black, like plumbago; but this certainly cannot be regarded as usual or in any way characteristic.

The discoloration does not extend uniformly over the surface. It seems that there is a general tendency to excessive formation and deposit of pigment, and it is probable that in many cases there is discoloration all over the body, though very faint excepting in those places which are most exposed, or where there is a natural tendency to the deposit of pigment.

Thus the face and hands are most frequently discoloured, and dark patches are also found about the genitals, in the axillæ and the popliteal spaces, and along the spine and the linea alba. These darker portions of skin gradually shade off into the surrounding lighter surface; very rarely do they pass abruptly into skin of normal colour. In Mr. L.'s case, the dark areas shaded gradually off into surrounding lighter skin, excepting on the hands, where the discoloration was abruptly limited on the sides. It is not rare to observe small spots of much darker colour upon the deeply discoloured areas. In addition, it has been frequently noticed that intense

discoloration is developed wherever an abrasion has occurred, or a blister has been applied, or wherever pressure has been exerted, as in the line of a strap worn over the shoulder, or of a dress-string around the waist.

The discoloration does not extend to the palms of the hands or the soles of the feet, though these have in some cases been observed to present dark spots. The roots of the nails remain free, and, indeed, owing to the coexisting anæmia, they are unusually white and present a very marked contrast with the dark colour of the back of the hand.

The discoloration often affects the mucous membrane of the mouth, and irregular bluish-black streaks or spots are frequently found on the lips and inside of the mouth, and more rarely on the tongue. Greenhow states that similar streaks exist in Lascars, thus supplying a further illustration of the resemblance between the pigmentation in Addison's disease and that which exists in the darker races of mankind. Niemeyer is inclined to regard these patches on the mucous membrane as pathognomonic of Addison's disease, since he finds no mention made of them in any of the recorded cases of bronzed skin without disease of the supra-renal capsules.

On the other hand, the conjunctivæ remain normal, and in only two cases have I found it recorded that they presented a peculiar dirty-brown colour. Small dark spots of pigment have also been noticed in the iris. Another singular illustration of the general tendency to excessive pigmentation, is the fact that the hair has been noticed to grow darker. Dr. Addison stated (*loc. cit.*, p. 215) that the irregular and excessive distribution of pigment was also occasionally manifest in the internal organs.

The mode of appearance of the discoloration is peculiar. It has been observed in cases where the symptoms have lasted only four months; but it does not usually appear among the early symptoms, and it certainly becomes most intense in slow chronic cases. It has frequently been noticed, and this was very well marked in Mr. C. L.'s case, that the colour varies considerably from time to time during the course of the disease. Allusion has already been made to the remarkable paroxysmal progress of this affection—periods of comparative ease and apparent improvement following the most alarming conditions. It is found that during or soon after (Bristowe) the exacerbation of the general symptoms, there is a marked deepening of the colour, while during the following period of remission the discoloration grows decidedly lighter. Not only so, but after the bronzing has become very marked in a certain place, it may fade away there, while some other area is growing much darker. The microscopic appearances of the discoloured skin will be alluded to under the head of morbid anatomy.

The skin is usually dry and harsh, and in some cases a peculiar disagreeable odour of the perspiration has been observed.

Having thus spoken of the peculiar symptoms of Addison's disease, it remains to allude briefly to its course and termination. Occasionally the

development of the early symptoms is more rapid and abrupt than usual, and the disease runs a rapid course, terminating fatally in a few months. It is probable, however, that in such cases, latent disease has been progressing in the supra-renal capsules for an uncertain length of time, and that finally an abrupt outbreak of the general symptoms has occurred. But in the more typical and ordinary cases, the course of the affection is a very chronic one, extending over from two to five or seven years, or even longer. Allusion has also been made to the remarkable alternations of apparent improvement and of rapid progress of the symptoms which are presented during this course, so that a patient whose condition appears almost hopeless may slowly rally, regain strength, and even be able to resume light occupation; in most instances, unfortunately, only to be abruptly reduced in the course of a few days to a condition of even greater prostration than at first by some apparently causeless attack of vomiting, diarrhœa, or some such disturbance. Several of these alternate paroxysms and remissions may be presented in the course of the disease. Finally, however, the patient sinks into a state of excessive prostration, the appetite fails, the pulse becomes extremely feeble and small, the temperature falls, there may be slight delirium, with a tendency to coma, or, on the other hand, convulsions may occur, and death follows from exhaustion. In some cases, death is preceded by a quite sudden and extreme collapse, not a little resembling that of cholera, excepting that there are no discharges, or at most only occasional vomiting. I would also call particular attention to the great liability to sudden death in Addison's disease. It is not uncommon in cases where the prostration is extreme for death finally to occur, as it did in Mr. L.'s case, very suddenly with or without some muscular effort to cause it. But it also occasionally happens that, in cases where the debility has not yet become so alarming, some rather excessive exertion may be followed by sudden and fatal syncope. Thus in an unpublished case, the details of which were communicated to me, the patient was removed from Philadelphia to Chicago, but died almost instantly on making some slight muscular effort after this fatiguing journey. So great is the danger of this fatal accident in cases of Addison's disease, that the relatives should be warned of the possibility of its occurrence, and positive injunctions be laid upon any unnecessary or unusual exertion.

The *prognosis* is almost invariably unfavourable as regards the final termination of the case; though life may be very greatly prolonged. In a few cases on record, very great improvement occurred, and, at the time of the report, had lasted so long as to give rise to strong hopes that it might prove permanent. Nor, so far as is known, is there any insuperable reason why recovery may not occur in Addison's disease. But as a matter of fact in nearly every case, if not in every one where the disease had been observed to the close, it has resulted in death.

Morbid Anatomy.—The lesions which are found after death from this affection are deserving of careful study. I have already spoken of the condition of the blood (p. 335), and will now call attention first to those appearances which are most constant and characteristic, and then to those which are less frequently met with.

The *skin*, where it is the seat of discoloration, presents the same conditions as are found in the darker races of men. The pigment, in the form of fine granular particles, is deposited in the rete mucosum, while the more superficial layers of the epidermis and of the true skin usually remain free from any coloration.

The lesions of the *supra-renal capsules* which are to be regarded as characteristic may be traced exclusively to a process of chronic sclerotic inflammation with caseous degeneration of parts of the newly formed exudation. It occasionally happens that true tuberculous granulations will be also found developed in the stroma of the gland surrounding the areas of cheesy degeneration. A minute description of these lesions will be found at page 83 (Mr. L.'s case), and I shall, therefore, in this place, merely sketch in general terms the different stages which the morbid process passes through, and the general and microscopical characters of each.

In the early stage, which is scarcely ever seen excepting in the cases which run a comparatively acute course, the capsules are enlarged and heavy; their envelope is usually inflamed and thickened. On section, the pigment layer, which is so marked in the healthy capsules, is absent, and there is no line of demarcation between the cortex and the medulla. If the process has involved the whole gland uniformly, the section may present a uniform grayish, semi-translucent structure. This is due to inflammatory hypertrophy of the interstitial fibro-cellular tissue, the gland elements having undergone atrophy. On microscopic examination, a finely fibrillated stroma is observed, with numerous lymphoid cells and nuclei. This corresponds to the first stage of sclerosis. A little later, the capsule is still enlarged as before, but a section presents a marbled appearance, the grayish, semi-translucent surfaces being dotted with irregularly-rounded, opaque, yellowish or cream-coloured patches, where fatty degeneration of the new-formed tissues has begun. The subsequent changes which the capsules undergo are familiar in other forms of sclerosis. The grayish, fibrillated stroma develops into a more and more dense fibroid tissue, contracting and causing puckering and shrivelling of the capsule. The patches of fatty degeneration undergo the various stages of retrograde metamorphosis. The fibrils disintegrate, the cells become shrivelled and filled with oily and granular matter. In some instances a process of fatty liquefactive change occurs which reduces the degenerating spot to a pseudo-cyst, filled with a diffluent, creamy matter, which is really of oily nature, though often erroneously described as purulent. Occasionally such cysts persist for a long time, and remain with

their peculiar fluid contents after other parts of the organ have passed into further stages of degeneration; but usually the fluid parts are slowly absorbed, leaving a dryish, friable, and cheesy residue. In other instances, this stage of cheesy degeneration is gradually induced without passing through the intermediate stage of liquefactive softening. Subsequently the organic portions of these cheesy collections are slowly removed by absorption, and more or less complete calcification results. It will be seen, therefore, that the affected capsules present different conditions, according to the duration and stage of the morbid process, although this is in all cases one and the same. It has already been mentioned that occasionally true tuberculous granulations are found in the stroma surrounding the areas of cheesy degeneration. This does not, however, justify the view that the morbid process is essentially a tuberculous one, since a similar development of tuberculous granulations, due to the infectious influence of areas of cheesy degeneration, is familiar as a secondary phenomenon in many localities. In the last stages of the change, as seen in typical chronic cases, the capsules are very irregular in shape, puckered and nodulated. They may be smaller than normal, owing to contraction and absorption. Their envelope is dense, thickened, and often closely adherent to adjoining parts. On section they present the various stages of degenerative change above described. In nearly every case (all but 4 out of 128 — Greenhow) both capsules are affected, but far more frequently it has not advanced equally in the two.

It will be seen that many of the symptoms of Addison's disease appear to indicate some implication of the sympathetic nervous system, or of the pneumogastric nerves, and accordingly, in a small number of cases, a careful examination has been made of the condition of the supra-renal and solar plexuses.

Considering the close proximity of the supra-renal capsules to the large abdominal nervous ganglia, and the fact that there is marked thickening of the envelopes of the capsules, as well as of the surrounding cellular tissue, it is but what might have been expected that the ganglia and plexuses should be invested with indurated and condensed tissue. In a few instances the fibrous tissue in the ganglia is stated to have been increased, with or without alteration of the nerve-cells. Examination of the nerve-trunks connected with these plexuses has also shown that the morbid process had extended to their sheaths, causing fibroid thickening with or without atrophy of the nerve-fibrils from pressure. It cannot yet be said, however, that such lesions are constant or even frequent, since careful examination of the parts has been made in but few instances; and, in some of these, with negative results. Thus, in the case of Mr. C. L., minute examination of the abdominal sympathetic nerves and ganglia revealed an entire absence of any lesion. It is much to be regretted that this point has not more frequently been examined with such care as to establish positively

the existence or non-existence of any definite changes in these nervous tissues, since, as will be seen later, one of the most popular theories for explaining the peculiar symptoms of Addison's disease rests entirely upon the serious complication of the sympathetic nerve. Apart from this, no lesions are known to occur in the nervous system, although careful examinations of the brain and spinal cord are still much needed.

Thorax.—The lungs very frequently present caseous nodules, surrounded by fibroid induration. Frequently, also, softening of the cheesy matter has occurred with the production of small cavities, such as I have described in Mr. C. L.'s case. The amount of lung-tissue involved may be limited to a patch one inch in diameter, or a considerable part of the upper lobes may be consolidated. The cavities are, as a rule, old, and there may or may not be a development of miliary tubercles in the surrounding tissues. In other cases, on the contrary, the lungs present the lesions of diffused miliary tuberculosis, resulting, I believe, from constitutional infection from the caseous nodules in the supra-renal capsules. In many cases, the existence of long-continued irritative action in the lungs is shown by the existence of old pleural adhesions and fibroid thickening of the pleuræ. It is unusual to find any pleural effusions. The *heart* has, unfortunately, not been often subjected to careful microscopical examination in this affection. In cases where it has, fatty degeneration of the muscular substance has generally been detected, as might be anticipated from the extreme anæmia and the evidences of failure of heart-power. There is no tendency to valvular disease. In a few cases, recent pericarditis has been found.

Abdomen.—Occasionally spots of excessive deposit of pigment have been observed on the peritoneum or in some of the viscera. Cellular adhesions may exist between different organs or between folds of intestine, and in cases where general tuberculosis has been developed, miliary granulations are apt to exist upon the peritoneum also.

The liver and kidneys are, as a rule, found healthy.

The spleen, though sometimes mentioned as healthy, is usually decidedly enlarged, swollen, and soft. Its colour is most frequently dark, so that it has been compared to the spleen in typhus fever; but in Mr. L.'s case I have noted it as *rather pale.*

The mucous membrane of the stomach is rarely healthy. In some cases enlargement of the gastric follicles is found, as described at page 84; in others a mammillated condition is observed, which is due, according to Coupland and Schäfer, to local outgrowths of lymphoid tissue. Small ecchymoses are occasionally found on the mucous membrane, and, more rarely, small abrasions or ulcers.

The intestine usually presents the evidences of chronic intestinal catarrh; and, although in the present case there was no enlargement of the solitary glands or of Peyer's patches, these lesions are present in very many

instances. I would call special attention to the numerous subperitoneal and submucous ecchymoses which existed in Mr. L.'s case (see page 84). Ulcerations are but very rarely found. The mesenteric glands are enlarged and occasionally caseous; in the present case they contained abnormal deposits of pigment, possibly the result of the ecchymoses above described. The retro-peritoneal glands in the neighbourhood of the supra-renal capsules may also be found enlarged, and in a state of cheesy degeneration.

Bones.—In a typical case of seven years' duration, reported by Gull (*Medical Times and Gazette*, October 21, 1865, p. 441), the patient had complained of pain in the left foot. At the autopsy, characteristic lesions of the supra-renal capsules in the last stage were observed. The bones forming the left ankle joint (tibia and astragalus), as well as others of the tarsal bones, were soft, and easily cut by the knife. On section they presented either a yellow (fatty) or a red appearance. None of the joints, including ankle joints, were at all diseased. No mention is made of the other bones. I trust that in future examinations the state of the marrow may be carefully determined.

Causes and Nature. Explanation of Symptoms.—It has been seen that the lesion of the supra-renal capsules, which is characteristic of Addison's disease, is a chronic inflammation of low grade, with sclerosis and cheesy degeneration. It is interesting to inquire what causes induce such a condition of disease in these organs, about whose functions our knowledge is so imperfect. It is evident that the affection is not primarily tuberculous in character; and, indeed, from an examination of the antecedents of patients, and from the age at which it chiefly occurs, it can scarcely be classed as scrofulous. It is true that Greenhow and others speak of it as frequently occurring in persons of a tuberculous diathesis; but this appears doubtful to me, since I should be inclined to regard the lung trouble as secondary, the result of infection from the cheesy, degenerating capsules. Indeed, it would seem that the number of cases in which general miliary tuberculosis has followed from such constitutional infection is very small relatively, so that it would not indicate that the subjects in whom Addison's disease has been observed were at all strongly predisposed to tuberculosis.

It appears from the analysis which Greenhow has published of nearly all cases on record that Addison's disease is far more frequent in the male sex, and occurs almost exclusively in those who are engaged in active manual labour, the cases being pretty equally distributed over the laborious period of life, and being almost entirely confined to that period. In a few instances the beginning of the disease has been referred to the occurrence of some strain or injury to the back; and, from the character of occupation of the vast majority of the patients, it is highly probable that such a cause may have very frequently existed without attracting especial attention. I would refer here to the marked pain which was experienced by

Mr. L., for years before the development of definite symptoms, whenever he engaged in such work as digging, which requires straining efforts with the back. Further, in a considerable number of cases, there has been chronic inflammatory disease of parts adjacent to the supra-renal capsules, such as caries of the vertebræ; and it is altogether probable that the latter disease was the primary one, and that the capsules became affected by extension of inflammation. It is, of course, impossible to decide in how large a proportion of all cases of Addison's disease the above direct causes are operative, and in how many instances, if at all, the disease arises from general constitutional causes alone. It is quite possible that there may exist in certain persons a peculiar tendency to this low grade of inflammatory action in the supra-renal capsules, which is readily excited by slight mechanical causes.

According to various writers climate would seem to play a marked part in the causation of Addison's disease. Thus it appears to be far most frequent in England, and then, according to Jaccoud, Italy, the Low Countries, Germany, and finally France follow. It is certainly a rare affection in America. Still I doubt if much value can be attached to any of these statements, since they are based merely on the proportion of all the recorded cases (but little over 300 in number) which has occurred in each of the respective countries. Before the true influence of climate can be determined, it will require a far larger range of observation, directed with equal attention, in the various localities. Hitherto the attention of the profession in England has naturally been closely directed to this subject, and, it is probable that, in consequence, cases have there been detected which elsewhere might have been overlooked. It must also be remembered that the real frequency of any affection must be calculated in relation with the number of inhabitants of each country; and especially with the extent of population in the large cities, from which the great proportion of records of such cases is drawn. It will be readily understood why a disease, plausibly thought to be due, in many cases, to strain or injury, should occur with comparative frequency in such a city as London, with its vast numbers of male inhabitants engaged in every species of hard work. It seems to me probable that climate will be found to have no special influence whatsoever.

If the causes of Addison's disease be not definitely ascertained, the relation between the lesion of the capsules and the characteristic symptoms of the affection are equally the subject of discussion.

In the first place it must, I think, be admitted that these symptoms are not directly dependent upon the disturbance or abolition of any function the supra-renal capsules may be supposed to possess. It has been shown by Harley and others (see *Brit. and For. Med.-Chir. Review*, 1856), despite the experiments of Brown-Séquard, that the supra-renal capsules

are not in any way essential to life, and that their removal leads to no definite disturbance.

The capsules may be the seat of other forms of disease, as hemorrhage, cancer, cysts, fatty degeneration, to such an extent as to lead to entire loss of the healthy structure, and yet without the development of the peculiar discoloration of the skin or the characteristic general symptoms. There are quite a number of cases which demonstrate this position; and I will merely give the following brief summary of a case in which cancerous nodules were found in the left supra-renal capsule, without the presence of discoloration or any characteristic symptom.

CASE I.—Sarah S. æt. 29 years, married but sterile, was in ill health during 1866, with symptoms of severe irritation of rectum and bladder, followed by the appearance of a hard tumour in left iliac region. In fall of 1867, symptoms of acute cerebral softening (attributed to presence of a cancerous tumour in brain) made their appearance, and death followed within a fortnight. There was marked emaciation, but no discoloration of the skin in any part.

At the post-mortem examination, a small tumour was found in the brain with red softening surrounding it. There was scirrhous cancer of left ovary. The right supra-renal capsule was healthy, the left was enlarged and hardened, and on section presented several nodules of scirrhous cancer. There were some old and quite firm local peritoneal adhesions.

It is evident from the stage which has been reached by the morbid lesion in some cases where the symptoms have existed for but a comparatively short time, that even extensive degeneration of the supra-renal capsules may occur before the development of any recognizable symptoms. And further, it appears from the record of a small number of cases, that when the disease has been limited to one capsule, the general symptoms and course of the case have not been different from those of the more common form where both capsules are affected, even if not to exactly the same degree.

As it seems indisputable, therefore, that the peculiar features of Addison's disease cannot be dependent upon the mere impairment or abolition of any function which the supra-renal capsules may possess; and yet as it is established beyond question, that the occurrence of the peculiar form of inflammatory degeneration of these organs which we have described, is the characteristic and primary lesion in Addison's disease; it becomes evident that the symptoms must depend upon some influence exerted by the diseased capsules upon the rest of the economy.

This brings us directly to consider the two principal ways in which such an influence may be supposed to be exerted.

The first of these, which has attracted a great deal of attention and favourable comment from some of the most distinguished investigators of this subject, is through the medium of the nervous connections of the supra-renal capsules. The second is by the slow induction of cachexia, with grave disturbance of the elaboration of the blood, and interference with general nutrition.

The first supposition is based upon the following data :—

1. The unusually rich nervous supply of the capsules.

2. The proximity of the solar plexus and the semilunar ganglia.

3. The connection of the nerves of the capsules with the phrenic and pneumogastric nerves.

4. The character of many of the principal symptoms which follow degeneration of these organs.

There has been a good deal of doubt about the exact anatomical structure of the supra-renal capsules, though all authorities agree as to the large number of nervous branches which are connected with them, and as to the existence of a certain number (probably quite small) of nerve-cells, in the central medullary substance. Some writers have been led, in consideration of this, to rank the capsules among the nervous structures; but the most elaborate and apparently reliable investigations, those of Grandry,[1] appear to finally decide their place to be among the ductless glands. It is not possible at present to assign any function to them, though it would seem from analogy, that they are in some way connected with the elaboration of the blood. It has been already seen that they are not essential to life.

It is evident, however, that if a chronic inflammatory process should extend from the capsules to the connective tissue surrounding them, and at the same time along the sheath of the nerve-branches connected with them, such a degree of hyperplasia and thickening might result, followed by such contraction and condensation of the affected tissues, as would seriously irritate and involve, and ultimately cause atrophy and degeneration of the nerve-branches and even of the solar plexus and the semilunar ganglia. It may even be conceived that, before any gross lesions of the sheaths of the nerves connected with the capsules, or of the cellular tissue investing the ganglia, should be developed, so much irritation of the terminal filaments in the capsules might exist as to give rise, by reflex action, to very marked results.

Granting that such irritation and such morbid changes should be present, it is not difficult to trace an explanation of some of the most characteristic symptoms of Addison's disease.

Thus the extreme muscular debility may be attributed to the prolonged reflex irritation of the nerve centres; the frequent action of the heart with small feeble pulse, and the disposition to breathlessness or even syncope on exertion may be referred to implication of the pneumogastrics and phrenics, or to irritation of the thoracic ganglia of the sympathetic; the irritability of the stomach with nausea and vomiting, and the occasional abdominal pain and diarrhœa would point to interference with the solar plexus and semilunar ganglia; and it is further possible, if certain experiments of

[1] Journ. de l'Anat. et de la Phys., 1867, pp. 225 and 389.

Pincus (quoted by Greenhow from Funke's Physiology) are reliable, that the evidences of catarrhal irritation of the mucous membrane of the stomach and intestine may depend upon the disturbance of these same great nervous ganglia. It has been shown by careful experiments (Jaschkowitz), that section of the abdominal sympathetic is followed by a moderate degree of swelling and enlargement of the spleen, such as is observed in a great number of cases of Addison's disease.

Finally, there is good reason to attribute the unusual tendency to pigmentary deposition in the skin, and elsewhere, to a morbid irritation of the nerves of the abdominal plexus. It has been already seen (see page 337) that there is no definite relation between the extent of the lesion of the supra-renal capsules and the degree of the discoloration; that discoloration of the skin is known to occur only in connection with chronic sclerotic and caseous inflammation of the capsules, while various other organic lesions of these organs occur without any such result; and that consequently it cannot be held that the bronzing of the skin depends upon the disturbance of the function of these organs.

The fact that Vulpian has found that the capsules and the blood passing from them contain a substance which yields a peculiar deep-blue reaction with perchloride of iron does not appear to have any special connection with the peculiar bronzing of the skin in Addison's disease.

Again, it is a perfectly familiar fact that very marked discoloration of the skin may be found in cases where the supra-renal capsules remain entirely healthy. In cases of hepatic or gastro-hepatic disease, or of chronic malarial fever, a discoloration of the skin may occur, which closely simulates that described in connection with Addison's disease. In cases of uterine disease I have known the bronzing of the skin to be so intense, and to occupy such positions as to give rise to serious doubts as to the nature of the case. So, too, where extensive disease of the abdominal organs exists, as in the case of cancer of the peritoneum and ovary reported by Dr. S. Weir Mitchell (*Amer. Journ. Med. Sciences*, Oct. 1867, p. 413), or as in the case of tuberculous peritonitis reported below by us, very marked bronzing or discoloration of the skin may occur. It is true that in most of these cases the discoloration differs either in locality or in arrangement from the bronzing which is characteristic of Addison's disease. It is also true that the peculiar stains on the inside of the lips, mouth, and tongue, are rarely, if ever, seen excepting in the latter affection. But still, so great is the resemblance sometimes presented, that it is necessary to conclude that local discolorations, without the characteristic general symptoms, should not be regarded as diagnostic of Addison's disease, and that even when the bronzing is marked and extended, we should hesitate about making a diagnosis of Addison's disease, unless no pathological condition of any organ (other than the supra-renal capsules) can be detected.

In considering the manner in which the discoloration of the skin is brought about in these various conditions, it appears that the only element they possess in common is irritation of the abdominal plexus of nerves. Accordingly, the explanation which is now generally accepted of the bronzing of skin in Addison's disease is that it is due to slow, progressive increase in formation of pigment under the influence of irritation of the vaso-motor nerves. One of the peculiarities of the discoloration—the fact, namely, that its intensity varies from time to time—would seem to be better explained upon this supposition than upon any other.

When now we pass from this to the consideration of the various other symptoms of Addison's disease already mentioned, it must be conceded that the view so ably supported by Jaccoud,[1] Greenhow,[2] and others, which refers these symptoms also to morbid irritation, or entire loss of function of the nerves connected with the supra-renal capsules, is entitled to careful consideration. Attractive as it is, however, I cannot feel, even with a full appreciation of all that has been urged above, that this theory of the disease is entirely satisfactory and sufficient. I do not doubt that many of the symptoms are due to such interference with the nervous system; but I incline to believe, also, that the element of constitutional infection from the foci of cheesy degeneration must also be taken into account.

It must be observed that the number of post-mortem examinations as yet recorded in which lesions of the abdominal sympathetic have been demonstrated are but few in number. It is true, on the other hand, that we have comparatively few cases recorded where it is distinctly stated that careful examination of the solar plexus and semilunar ganglia revealed no lesions. In the case of Mr. C. L., however, it will be seen (p. 84) that careful study, both of the gross and microscopic structure of the abdominal sympathetic, gave purely negative results. It is difficult, therefore, to comprehend how such a perfectly healthy condition could have been maintained if the very marked and characteristic symptoms which existed for several years were dependent chiefly upon morbid irritation of these nerve-ganglia and branches. At the same time, it may very well be believed that the thickening and induration of the envelope of the supra-renal capsules and of the surrounding cellular tissue which existed might produce enough reflex irritation of the sympathetic ganglia to aid in the development of some of the more purely nervous symptoms of the case. It is to be observed, also, that in Mr. L.'s case certain phenomena which would seem to be most plausibly referred to mere nervous irritation, were not so marked as is usual in equally characteristic cases.

[1] Nouv. Dict. de Méd. et Chir. pratiques, t. v., 1866. Article, Maladie Bronzée.

[2] On Addison's Disease, Croonian Lectures for 1875.

Further investigations are necessary before a positive opinion can be pronounced, but it would certainly appear to be established that in Addison's disease some of the symptoms are dependent upon interference with the ganglia of the abdominal sympathetic, and with other nerves connected with the supra-renal capsules; and it seems probable, also, that the amount of this interference varies in different cases, and that, in consequence, the comparative prominence or slightness of certain symptoms will result.

It is necessary now to consider the symptoms from the other standpoint, and to discuss how far they may bear explanation on the view that Addison's disease is a cachexia, attended with grave disturbance of the elaboration of the blood, and interference with general nutrition.

In the first place it may be well to regard for a moment the evident analogies between the symptoms of Addison's disease and those of other cachexiæ, in which the existence of a special nervous element has not been suspected. In the article published in this Journal in October, 1875 (p. 313), I expressed my belief in the essential identity of the various forms of leukæmia, with so-called progressive pernicious anæmia; and endeavoured to show that the differences between the symptoms of the several forms depend chiefly upon the special organs affected in each. If, now, we compare the symptoms of progressive pernicious anæmia, or anæmatosis, as I have proposed to call it, with those of Addison's disease, a considerable degree of correspondence will be noticed.

Progressive Pernicious Anæmia, or Medullary (?) Anæmatosis.	*Addison's Disease.*
Insidious and apparently causeless development of languor, debility, and pallor of surface; weak, small pulse; tendency to palpitation of the heart, to attacks of dyspnœa, to giddiness and tinnitus, and later to dangerous and even fatal syncope.	Progressive, apparently causeless languor and debility, with, in most cases, bronzing of the skin; weak, small pulse; palpitation of the heart and breathlessness on exertion; faintness, and even tendency to dangerous or fatal syncope on exertion; giddiness and tinnitus occasionally observed; so also tremors, partial anæsthesia or numbness, or even convulsions.
Failure of appetite; sense of pressure or discomfort at the epigastrium; attacks of nausea and vomiting.	Failure of appetite; epigastric distress; spells of nausea and vomiting.
In some cases slight, irregular, febrile action. Temperature sometimes normal throughout.	Febrile action very rare; temperature normal, or even reduced.
Absence of emaciation in any marked degree.	Absence of emaciation in any marked degree.
Occurrence of hemorrhage from nose, gums, etc., or of petechiæ under skin, or under serous membranes.	Hemorrhages do not occur. Petechiæ not rarely found after death.

Progressive Pernicious Anæmia, or Medullary (?) Anæmatosis.	*Addison's Disease.*
Albumen not found in my own cases, but reported to be occasionally present.	Albumen not present.
Strong anæmic murmurs over heart and great vessels very constant.	Anæmic murmurs occasionally met with, but not frequent.
Progressive reduction of the mass of the blood, and especially of the proportion of red globules.	Progressive reduction of the mass of the blood; proportion of red globules not specially diminished; increase in proportion of white corpuscles.
Steady progress of debility; the occurrence of wandering delirium, or increasing coma, and finally death. Occasionally, sudden fatal syncope.	Steady progress of debility; wandering delirium; increasing coma, or, in rare instances, convulsions, and finally death. Occasionally, sudden fatal syncope.
Enlargement of spleen, of solitary glands of intestines; ecchymoses; fatty degeneration of heart, liver, and kidneys. Passive serous effusions.	Enlargement of spleen, of solitary glands of intestines, of gastric follicles. Ecchymoses occasionally. Fatty degeneration of heart frequent. Serous effusions rare.
Lesion of marrow of bones, in some cases at least.	Marrow not yet examined.
Occasionally a centre of chronic suppuration.	Chronic inflammation, with cheesy and sclerotic degeneration, and of suprarenal capsules constant.

It appears to me impossible to consider carefully the resemblance thus sketched between the symptoms and course of these two affections, without being struck by its closeness, and being led to inquire whether it may not be possible that there is something in common between them. In speaking of progressive anæmatosis, I have attempted to explain the symptoms there met with, by referring them to the diminution and deterioration of the blood, and the failure of cardiac power from fatty degeneration, and from impaired nervous force. And I think it will be noticed that very many of the symptoms of Addison's disease admit of a similar explanation.

It is true that the bronzing of the skin prevents the development of the familiar anæmic appearance, but in some cases the disease is well advanced or death may even occur before bronzing of the skin appears, and in such cases the appearance of anæmia is very manifest; while in all cases the conjunctivæ and the matrices of the nails are extremely pale and anæmic. The reduction in the amount of the blood and the increase of white corpuscles have been already referred to, and although the colour of the blood remains good and the red globules, while absolutely deficient, do not seem to undergo any great proportionate reduction, it seems altogether probable to me that some grave defect in the elaboration of blood exists. Some of the more usual nervous symptoms (tinnitus, vertigo, etc.) may be plausibly referred to the condition of the heart's

action, and to the cerebral anæmia due to the reduction of the mass of the blood; while others (such as tremors, partial numbness or anæsthesia) may, perhaps, be more properly referred to reflex nervous irritation; though it is not impossible that these as well as the convulsions which are noticed in rare cases may be due to the state of the nervous centres. The weak, small pulse, readily accelerated by exertion; the feeble action of the heart; the breathlessness on exertion; and the tendency to syncope, are certainly capable of plausible explanation by the frequent existence of fatty degeneration of the heart and by the anæmia of the nervous centres. I would again refer to the remarkable resemblance between the progressive and extreme muscular debility which attends both pernicious anæmia and Addison's disease, and which would seem to be explicable by a similar condition of the brain and spinal cord.

But it is not desirable, at the present time, to go more into detail in an attempt to show how plausibly many of the symptoms of Addison's disease might be explained without invoking the element of irritation of the abdominal sympathetic nerve.

Important evidence in favour of the view that there is also in Addison's disease an element of constitutional infection with impairment of blood-elaboration is to be drawn from the anatomical changes. Much light has been thrown of late upon the gradual influence of foci of chronic suppuration or cheesy degeneration in producing infection of the constitution, with the development of secondary cheesy deposits, or even, in cases where the predisposition exists, of general tuberculosis. And in Addison's disease, in connection with the chronic inflammatory changes in the supra-renal capsules progressing slowly during years, we find, in the enlargement and occasional cheesy degeneration of the neighbouring lymphatic glands and of the mesenteric glands; in the swelling of the spleen; in the enlargement of the gastric follicles and of the solitary glands of the intestines; in the increase of white corpuscles of the blood with reduction of its mass; in the very frequent occurrence of secondary cheesy deposits in the lungs, and occasionally of general tuberculosis, a train of pathological changes which is certainly suggestive.

I do not desire to be understood as offering such an explanation of the pathology and symptoms of Addison's disease in place of the one now generally received in which the symptoms are so largely referred to implication of the abdominal nerves and ganglia. But I wish to call attention anew to the importance also of the blood-changes and the signs of constitutional infection in this disease; and to the necessity for careful study of the splenic pulp, and especially of the marrow of the bones, in order to discover whether there is any such lesion there as has been found to exist in progressive pernicious anæmia and medullary leukæmia.

I do not think the microscopic examinations of the blood and tissues have yet been sufficiently numerous and accurate to enable a positive

opinion to be expressed; but I incline to the belief that the essential pathology of Addison's disease may prove to embrace both elements, as follows: a primary chronic degenerative inflammation of the supra-renal capsules; constitutional infection, with production of secondary caseous deposits (or, in some cases, of tuberculosis); impairment of the blood-elaboration (anæmatosis), possibly with lesion of the marrow of the bones or of the splenic pulp; consequent fatty degeneration of the heart; extension of irritation from the capsules to the nerves connected with them, to the semilunar ganglia and to the solar plexus. These factors are not stated in what is supposed to be their order of occurrence, or of relative importance in regard to the production of the symptoms of the disease, and it is evident that upon the predominance of one or the other will depend certain peculiarities of individual cases.

Diagnosis.—Many of the questions connected with the diagnosis of Addison's disease may be dismissed with a brief reference only. I have already called attention to the fact that in some cases the development of the muscular debility is so sudden and marked as to give rise to the suspicion that the patient is about to have an attack of typhoid fever. In Mr. L.'s case, his family, who were observant and experienced, were impressed with this belief. But although in a case seen for the first time in one of the sudden spells of prostration, or in a case where the constitutional symptoms make their appearance abruptly, such a doubt might exist for a day or two, a careful study of the peculiar symptoms, an examination of the history of the case, and the absence of the characteristic features of typhoid fever would soon enable a positive diagnosis to be established.

In some cases of pityriasis versicolor or nigra, the patches of discoloration are of much the same shade as is observed in Addison's disease. But here, in addition to the absence of all the peculiar constitutional symptoms, the discoloration does not affect the same localities as in Addison's disease, there is a sharp line of demarcation between the healthy and the discoloured skin, the surface is covered with a fine furfuraceous desquamation, and there are no pigmentary deposits in the mucous membrane.

It is only necessary to mention the fact that the staining of the skin from the prolonged use of nitrate of silver has been mistaken for the bronzing of Addison's disease. In reality it would be difficult to make such a mistake, not only on account of the different colour and distribution of the staining, but also on account of the absence of any of the characteristic general symptoms.

We come now to the more difficult question of distinguishing between Addison's disease and other affections attended with bronzing of the skin. It is true that in these latter cases the discoloration rarely presents the same distribution as in Addison's disease, and also that there are no dark streaks on the mucous membrane of the mouth. But still, these latter are not constant in true Addison's disease, and, in some instances, it

would be impossible to make a differential diagnosis from the characters of the discoloration alone. In such cases we should turn to the constitutional symptoms, a careful study of which will generally enable a correct diagnosis to be made. The following interesting case is reported, however, to show how closely even these may be simulated by other conditions :—

CASE II.—Lydia B., æt. 30 years, single, was admitted to the medical ward of the Philadelphia Hospital, April 4, 1870. She had been sickly from childhood, having had smallpox, typhoid fever, and several pleuritic attacks. No history of syphilis. She had not menstruated regularly since March, 1869, and not at all for two or three months past. Three months before her admission she noticed a brownish discoloration of the skin just below the right breast. This extended so as to cover breast, abdomen, and back. At first it was of very light colour, and gradually grew darker. During this time she was not sick, though still delicate and weak. On April 2, 1870 (ten days before admission), she was attacked with a chill, sharp pain in the side, fever, and loss of appetite. The symptoms soon subsided under appropriate treatment, but a second attack occurred in a fortnight, after which she continued very weak and almost entirely confined to bed. She had occasional severe attacks of digestive disturbance, failure of appetite, vomiting, and diarrhœa. There were also progressive emaciation, frequent complaints of pain in the lower part of the left side of the chest, and great weakness. On August 20th she was put on a diet of skimmed milk, beginning with f℥iss q. t. h., and increasing gradually till she took Oj t. d. Her attacks of vomiting ceased, but she still had occasional diarrhœa, lasting for a few days.

Oct. 10, 1870. A few weeks ago the discoloration of the skin had faded on the front of the trunk, in some parts having almost disappeared, but it is again growing darker. The position of the darkest discoloration is below the umbilicus and over the hypochondria, and from these points the tint gradually shades off, merging into the lighter intermediate portions. The linea alba is very dark. The dorsal surface of the trunk presents quite uniform dark-brown discoloration, beginning over sacrum and extending upwards to level of second lumbar vertebra, where it shades off very gradually to the colour of the remaining part of the back, which is decidedly darker than normal. There are numerous scattered spots of dead white skin (vitiligo) over the back. These vary in size from 1 to 4 lines in diameter, and are usually ovoid in shape.

There is also a large discoloured patch, mottled with whitish spots, on the anterior part of each thigh, reaching nearly up to the groins, which are not discoloured. There are no spots of vitiligo on abdomen.

The face is sallow and dingy, but the conjunctivæ remain clear, and are pearly white. There is no discoloration of the hands, the axillæ, or of the popliteal spaces. There is, however, marked discoloration of the outer surface of arms from wrists up to shoulders. In several places where blisters have been applied there is very intense discoloration.

The emaciation is not yet extreme, but there is very great loss of muscular power, so that she is scarcely able to walk, and even on attempting to get up she suffers from vertigo and faintness. A walk of even fifty yards causes great prostration, violent palpitation of the heart, and dyspnœa. She consequently scarcely ever leaves the bed.

There are no marked nervous symptoms, except such as depend on the extreme anæmia and debility. The mind is clear, and she does not suffer from headache. She does not dream much, and usually sleeps fairly, though some nights she is very restless.

The tongue is clean and moist, the bowels are now quiet. There is complete absence of appetite.

For past two weeks there has been a painful swelling above the styloid process of the right radius, which is the seat of rheumatoid pain, worse at night.

There is frequent, dry, hacking cough, without expectoration. There is

some tenderness, with sharp pain on coughing or deep breathing over lower part of left thorax. There is no dulness on percussion. There is blowing breathing with prolonged expiration at the right apex. At the left apex there are some crackling râles; and over left chest are friction sounds which vary in position and character. Respirations are not much accelerated except on exertion.

The cardiac sounds are normal. The pulse varies from 85 to 115, is regular but small, quick, and feeble. No hectic fever. There is no complaint of pain in abdomen or in loins. The urine is passed freely and is normal. There is no œdema.

21*st*. Less pleuritic pain. Debility increasing, so that after walking a few steps she suffers from vertigo, dyspnœa, and palpitation. No syncope. Sleeps poorly, without apparent cause. There is utter anorexia, and occasional diarrhœa.

Nov. 23. Physical signs much the same. No dulness; râles near root of right lung. Emaciation and debility increasing. For past four days there has been frequent and causeless vomiting. There is now considerable tenderness over the stomach. The discoloration of the abdomen has grown much lighter; and so has that of the back, though to a less extent.

Her treatment has consisted of quinia and cod-liver oil, which has been well borne by the stomach except during the attacks of vomiting. The vomiting has yielded most readily to small doses of morphia and chloroform, or of creasote. Her diet has consisted of milk, beef-tea, eggs beaten up with milk and whiskey; but no solid food.

Dec. 14. Has had another attack of vomiting lasting three days; vomiting a clear, slightly acid fluid three times daily. Bowels regular. She has but little cough. Emaciation is advanced, and debility extreme, dyspnœa occurring on slightest exertion. She has not, however, a sense of profound feebleness. She sank steadily, and died December 21, 1870; œdema of the right leg having supervened.

Post-mortem Examination.—Body extremely emaciated. Discoloration of abdomen very much diminished; that of back less so. Discoloration of thighs persists. The œdema of the right leg and right labium is still present. The brain and cord were not examined.

Thorax.—Heart small, but healthy. The lungs showed patches of adhesions here and there. On cutting into them, numerous disseminated patches of cheesy consolidation were found. These patches were, for the most part, superficial, covered by a layer of healthy vesicular tissue, and showed no softening; in a few places, however, central softening had occurred and led to small vomicæ.

Abdomen.—Liver fatty, pale yellowish in colour. Spleen somewhat enlarged; capsule much thickened and adherent to abdominal wall: pulp apparently healthy. The kidneys were healthy. The supra-renal capsules were also healthy.

There was diffuse peritonitis with matting together of the folds of the intestines. The peritoneum was thickened, and was studded over with numerous small grayish-yellow granulations.

The sympathetic ganglia of the abdomen were carefully examined, and presented a healthy condition. The entire body was intensely anæmic.

Unfortunately no microscopic examination was made of the blood or of the marrow of the bones.

It will thus be seen that bronzing of the skin is of comparatively little value in the diagnosis of Addison's disease, without the presence of the characteristic general symptoms. It appears also that, since both the general symptoms and the bronzing of the skin may be produced by other serious abdominal lesions, it is necessary to determine that there is no such condition present (as tuberculous or cancerous peritonitis for instance) before deciding that the case is truly one of Addison's disease of the supra-renal capsules. If it be true, then, that both the bronzing

of the skin and the general symptoms may be closely simulated in cases of other serious abdominal diseases, it would follow that we have a certain very peculiar group of symptoms, often attended by bronzing of the skin, which are believed to be due to conjoined impairment of the elaboration of the blood (anæmatosis) and irritation of the abdominal sympathetic and pneumogastric nerves; and which may apparently be caused by various local lesions, but especially by chronic degenerative inflammation of the supra-renal capsules. It is only necessary to refer to the comparison of the symptoms of Addison's disease and of progressive pernicious anæmia (anæmatosis) given at page 350, to appreciate the difficulty which would exist in distinguishing between the two, if it were not for the bronzing of the skin. Indeed I must confess that I see no means by which a positive diagnosis could be established in the absence of that symptom.

When we recall the fact that bronzing of the skin is not an essential symptom of Addison's disease of the supra-renal capsules, but gains its significance only in connection with the peculiar constitutional symptoms; it would seem desirable that so soon as the true nature of this peculiar group of phenomena (so closely analogous to those of progressive pernicious anæmia, and which are closely simulated in some other forms of abdominal disease) is clearly understood, some new term which may seem appropriate—*anæmatosis with bronzing of the skin*, or whatever else it may be—should be chosen to designate it. Until then, it is more convenient to retain the term Addison's disease, although in reality this should be restricted to the peculiar anatomical lesion of the supra-renal capsules first connected with these symptoms by Dr. Addison. This view seems to me of very great importance, because it widens and enlarges our conception of the nature of these constitutional symptoms which form a well-marked group, and which may be developed by chronic degenerative changes in the supra-renal capsules or by other irritative morbid processes in the abdominal organs.

Treatment.—Having already spoken of the prognosis, duration, and modes of termination, it remains only to speak of the treatment. Unfortunately there is but little of definite character or value to be stated. Many remedies have been recommended and tried, but in almost every case on record the case has progressed inevitably to a fatal issue. In some instances, temporary benefit has been thought to follow the use of some plan of treatment; but when we bear in mind the remarkable remissions which occur in the ordinary course of the disease, it is evident that great care must be used in forming any such conclusions. It cannot be doubted however, that it is possible to prolong life and relieve some of the symptoms by appropriate treatment; and in a very small number of cases it is possible that the progress of the disease has been checked, at least, for a considerable length of time, if not permanently. It will be remembered that at several periods in Mr. L.'s case, decided improvement occurred,

though only once did it last long enough to offer any encouragement as to the effect of his remedies, which were at that time nitrate of silver and iodide of iron, with faradization.

One of the most important elements in the treatment is *rest*. So long as any threatening symptoms of debility are present, the patient should remain in bed, and during the periods of temporary improvement, he should indulge but very cautiously in any exertion. This rule is not only important as tending to prevent excessive fatigue and relapses, but on account of the danger of sudden death from collapse, if any over-exertion is permitted.

It is probable that prolonged counter-irritation over the region of the supra-renal capsules might be productive of some relief, but I do not know that it has been tried sufficiently to justify any expression of opinion.

One of the most important indications is to avoid gastric disturbance, which is best effected by careful attention to diet. No general rule can be laid down upon this subject, owing to the capricious state of the appetite and taste which is often present. In most cases milk, with or without lime-water, may be freely given with advantage; and at times an exclusive milk diet affords relief. More often it becomes necessary to vary the diet from time to time, choice being made especially of simple, nourishing and digestible articles of food. The condition of the bowels is usually one of moderate constipation; but great care must be observed in the use of purgatives, owing to the dangerous prostration which is apt to follow their action. If it be impossible, therefore, to secure a sufficiently regular state of the bowels by laxative articles of diet, recourse should be had to simple enemas or to mild vegetable laxatives. During the attacks of gastric disturbance, attended with nausea and vomiting, which occur from time to time, the diet must be restricted to the administration at short intervals of small quantities of milk and lime-water or of beef-juice; associated with the use of iced seltzer water, iced dry champagne, powders of subnitrate of bismuth, etc. I obtained the most marked benefit, during these severe attacks in Mr. L.'s case from the use of chlorodyne in repeated doses. It may be necessary, owing to the obstinacy of the vomiting, to resort to the temporary use of nutritious enemas.

Another important indication is to increase muscular strength. It is true that this is essentially connected with the disease, and probably depends upon the anæmia as well as upon the exhaustion of the nervous centres by reflex irritation, and consequently its rational treatment would resolve itself into the treatment of the primary disease itself.

The use of strychnia appears indicated; but I do not know that it has been found of service. I have employed it but for a short time with negative results. The remedy from which I found most advantage in this direction was undoubtedly faradization with mild currents. Bearing in mind the liability to fatty degeneration of the heart, I should recom-

mend the occasional use of digitalis, especially in those cases where a tendency to spells of palpitation and dyspnœa on exertion is marked. Alcohol should be administered in small quantities, and in whatever form is best tolerated by the stomach.

The great indication in the treatment, however, must certainly be to endeavour to modify the morbid process in the capsules and surrounding tissues, and to counteract, so far as possible, the interference with the elaboration of the blood.

Among the remedies which prove most beneficial are, as might be expected, cod-liver oil, iron, phosphorus, nitrate of silver.

Iron especially should form an element of the treatment. I do not know that the form in which it is administered is of great consequence, provided that it be well borne by the stomach. Greenhow strongly recommends the tincture of the sesquichloride, ♏xv to xx, with chloroform ♏xv to xx and glycerin ℥ij. The iodide of iron would also seem likely to be of much value.

Phosphorus, which was strongly recommended by Broadbent in the treatment of leukæmia and allied affections on account of its supposed power of influencing the elaboration of the blood, has not been approved by the results of more recent and extended experience. It may be said, however, that this drug is still deserving of a careful trial in Addison's disease.

Nitrate of silver may be given with at least temporary advantage, especially in cases where irritability of the stomach and bowels exists, probably associated with chronic follicular catarrh of the mucous membrane. It is not unreasonable to believe that it may also produce a favourable alterative effect upon the chronic inflammatory process going on in the capsules and the surrounding cellular tissue. I used it in Mr. L.'s case, simultaneously with the iodide of iron, and with apparent marked benefit.

ART. III.—*The Proper Treatment of Pelvic Effusions.* By D. WARREN BRICKELL, M.D., Prof. Obstetrics, etc., Charity Hospital Medical College, New Orleans.

ACCORDING to my observation, pelvic inflammations are quite common, and they are not confined to married or child-bearing women. As distinct a case of pelvic cellulitis as I have ever seen—one requiring operation for its relief—was that of a virgin female from an adjoining State.

The diagnosis of these inflammations in their primary stages I believe to be a matter of considerable difficulty to the general practitioner whose attention is not at all carefully directed to the special affections of women. Many of the cases assume from the beginning the phase of severe rectal,