vertiginous sensations, the hæmorrhagic diathesis, must awaken suspicion as to the character of the malady, before the splenic disease manifests itself.

Treatment.—Unfortunately, we possess no specific against this disease, and hence the treatment must be symptomatic. Iron, which is a specific in anæmia, has no influence of a curative kind in leucocythemia, but it is useful as supplying a material needed in the process of repair. There are several remedies which affect the spleen, in a way which indicates a specificity of action: they are quinia, ergotin, and electricity. Quinia, iron, and ergotin can be given together in pill-form—five grains of quinia, one grain of reduced iron, and two grains of ergotin, should be administered three times a day. Simultaneously, electricity can be applied in the form of faradic electricity to the splenic region, or by means of an insulated electrode in the rectum, and the other over the spleen. A slowly interrupted galvanic current is, the author believes, more efficient. Good results are obtained from the local application of the ointment of the biniodide of mercury—unguentum hydrargyri iodidi rubri—to the splenic region. The ointment should be thoroughly rubbed in while the direct rays of the sun are falling on the part, or before a bright fire. The ointment is rubbed in daily, until the skin begins to vesicate, when it must be discontinued, but resumed again when the skin has recovered from the effects of previous applications. As the breathlessness on exertion, the vertigo, the mental troubles, the effusions, the hæmorrhages, etc., are due to the impoverished blood, attention must be directed to the central lesion, rather than administer remedies for individual symptoms. In some cases good results have apparently followed tranfusion of blood; but they were examples of the hæmorrhagic diathesis, rather than of true lencocythemia. In the latter disease transfusion is useless—three cases in which it was employed by Stoll, of Wurzburg, having proved fatal. As the function of blood-production is at fault, attention to the first steps in the process is necessary: in other words, careful alimentation is of great importance. Whether the appetite be languid or voracious, to insure thorough digestion, pepsin and muriatic acid should be administered after each meal. As, in the progress of the disease, the liver and intestinal glandular apparatus are disabled, fats, starches, and sugars should be excluded from the diet as far as possible, and the patient be fed on fresh meats, milk, eggs, and fish. Cases not yielding to the plan above indicated may be treated with arsenic, arseniate of iron, especially Fowler's solution, and the phosphates or compound sirup of the hypophosphites. These remedies should, of course, be pushed, especially the phosphates, for no immediate results can be obtained from them. Arsenic has been administered hypodermatically, and injected directly into the substance of the enlarged spleen with asserted advantage.

ADDISON'S DISEASE—MELASMA SUPRARENALE.

Definition.—Dr. Addison, of Guy's Hospital, in London, in 1855 announced the discovery of a disease in which, with a peculiar bronze-like discoloration of the skin, there are associated great weakness and anæmia, the whole being due to disease of the supra-renal bodies. His name has, by common consent, been associated with this disease permanently, which is hence known as *Addison's Disease—Morbus Addisonii.* It is sometimes called "the bronzed-skin disease," "melasma suprarenale," etc. It may be defined, in the words of Averbeck,* as "a well-marked constitutional disease, exhibiting itself locally as a chronic inflammation of the supra-renal capsules, but in its essence consisting in a peculiar anæmic condition, always tending toward death, which is characterized by intense development of pigment in the cells of the rete Malpighii and in the epithelium of the mucous membrane of the mouth."

Causes.—Although the anatomical structure of the supra-renal bodies has been successfully studied, the knowledge of their physiological functions has not advanced correspondingly. It is, therefore, difficult, even impossible, to trace a relationship between symptoms of the disease and some observed lesion. It occurs rather more frequently among men, and is a disease of adult life, no case occurring before ten or after sixty years of age. Dr. Greenhow† has collected one hundred and nineteen cases in males and sixty-four in females, of whom eleven years was the youngest, and fifty-nine the oldest, age at which death occurred. There is, however, an exceptional case in which the limit of maximum age is exceeded—that of a woman who is reported to have died at sixty-nine. Various depressing moral emotions and evil hygienic influences have been assigned a causal relation to the disease. Grief, anxiety, fear, exposure to cold and dampness, and want, are supposed exciting causes. A considerable proportion of the cases have coexisted with tuberculosis in other organs, and a few well-marked examples of the disease have been apparently due to a tubercular degeneration of the supra-renal bodies; hence the strumous constitution or diathesis is supposed to be intimately related to the disease. In Averbeck's collection of fifty-one cases, there were evidences of tubercular, strumous, or caseous degeneration in thirty-six. Greenhow holds that the condition of general tuberculosis, without being necessarily causative, frequently coexists with Addison's disease, and that "in a certain small number of cases the genuine lesion in the capsule has been found coexisting with advanced phthisis or general tuberculosis." It seems clearly established that Addison's disease is frequently associated with inflammation and suppuration in

* "Die Addison'sche Krankheit," Erlangen, 1869. (Merkel.)

† "The Croonian Lectures for 1875," "The Lancet," vol. i, 1875.

neighboring structures—extending to and ultimately involving the supra-renal bodies. Caries of the vertebra, psoas and perinephritic abscess, etc., are examples of such causes. Greenhow insists on traumatism as an influential factor, but this must be regarded as an exciting cause. A considerable proportion of cases occur without any obvious reason for their appearance.

Pathological Anatomy.—The condition of the supra-renal bodies varies with the period of the disease at which the examination is made. Virchow* describes a cheesy degeneration, beginning in the medullary tissue as small gray nodules, which gradually increase in size, amalgamate, and ultimately become caseous. A portion of the body may remain normal, or, gray nodules forming also in the cortical tissue, the whole organ may finally degenerate into a firm, caseous mass. The English authorities, especially Wilks and Greenhow, maintain that the disease in the supra-renal bodies is a low form of inflammation, during the course of which these organs become infiltrated with a fibrous exudation that undergoes conversion into a purulent, caseous, or cretaceous material. According to Merkel, the process is essentially tubercular. The nerves having intimate relations with the supra-renal bodies are also affected by a low grade of inflammation, consisting in congestion of the neurilemma, hyperplasia of the connective tissue, atrophy, fatty degeneration, and pigmentation of the ganglion-cells. The capsules which are in close proximity to the solar plexus and semi-lunar ganglia are more abundantly supplied with nerves, relatively to their size, than any organs in the body. The cells of the medulla present a strong resemblance to the multipolar ganglion-cells of the brain and spinal cord, and a number of nerve-trunks pass through the cortical portion into the medulla (Leydig). From this anatomical disposition it is maintained that the medulla is a portion of the ganglionic nervous system, while the cortex is a vascular gland (Kölliker). The nerve-trunks are invaded by contiguity by the inflammation attacking the capsules. The fibers and ganglia of the solar plexus are also changed. The neuritis, beginning in the nerves of the supra-renal bodies, extends to the fibers of the plexus and to the semilunar ganglia, the cells of which become cloudy and granular and pigmented, with subsequent atrophy. Traces of old and recent hæmorrhages are also found.

The blood is by some said to be deficient in fibrin and to have an excess of white globules, and the red globules do not manifest any tendency to form *rouleaux*. Greenhow finds that the blood does not exhibit any appreciable alteration in typical cases, and that the changes observed by Buhl and others were due to coincident but accidental lesions in the lymphatic glands. Atrophy and fatty degeneration of the heart and of the intima of the vessels have been observed in some

* "Krankhaften Geschwülste," Band ii, p. 689.

cases. The urine is deficient in urea and in pigment, and contains an excess of indican. The most striking change during life—the abnormal pigmentation—is due to the deposition of granular pigment in the cells of the rete Malpighii, in the papillary portion of the cutis, and even in the connective-tissue corpuscles. No change occurs in the proper structure of the skin. Similar pigment deposits occur in the mucous membrane of the mouth, especially along the edges of the teeth, while the conjunctiva, the nails, and the skin of the palms and soles of the feet are entirely free from deposits. It is obvious that the phenomena of Addison's disease—the anæmia, the feebleness, and the bronzing of the skin—are due to changes in the supra-renal bodies or in the connected nerves or ganglia. That alteration of the capsules will produce such symptoms can not be admitted, in view of the fact that cancer and other forms of degeneration have destroyed these bodies without causing this malady. It is the peculiar lesion of the supra-renal capsules, of the connected nerves, and of the solar plexus, with the semilunar ganglion only, that really produces the morbid complexus of Addison's disease. Unquestionably the changes in the nerves and ganglia are the most important pathological factors, and to them are ascribed the strange constitutional symptoms, including the pigmentation, by the chief authorities who have discussed the pathology of this malady. The view that the abnormal pigmentation occurs through the medium of the nervous system is supported by the fact that the discoloration lessens with improvement in the constitutional state, and deepens and extends when the symptoms indicate a more active condition. Analogous influence of the nervous system is seen in those cases in which a permanent darkening of the skin has followed sudden fear and agony of mind (Greenhow). It is the trophic system, especially, which is concerned. Doubtless Jaccoud nearly expresses the correct pathology when he holds that in Addison's disease the changes in the supra-renal bodies excite an irritation of the vaso-motor (trophic ?) system, which requires a much longer time to produce the pigmentation than to develop the asthenia ; hence the long existence of the latter before the appearance of the former.

Symptoms.—Addison's disease develops very gradually—so gradually that the time of beginning escapes observation. First, an unwonted sense of weariness on exertion is experienced. The debility slowly, in some exceptional cases quickly, increases, until a marked degree of asthenia is reached. There is not a corresponding degree of anæmia and wasting, and, although the sclerotic is pearly, the mucous membrane is red, and the blood has the normal proportion of red globules, while the subcutaneous fat is little if at all diminished, the muscles being weak and flabby. Disorders of digestion succeed to the early symptoms of debility. An unpleasant distention of the stomach is felt after eating ; eructations, nausea, and occasionally vomiting oc-

cur ; and during, sometimes between, the acts of digestion, considerable pain is felt in the stomach. Pains of a dragging, tearing character also occur in the hypochondria and in the spine, extending into the sacrum. Much tenderness is elicited by pressure in the hypochondria, especially in the right, where, besides, the pain is most acute. The joints also become the seat of considerable pain, which is increased by movement, but they are neither swollen nor tender. These pains are pretty constant, while the disorders of digestion are at first intermittent, becoming more and more frequent as the case progresses.

With the development of these symptoms the asthenia increases. The least exertion induces an overpowering sense of fatigue. An extreme pallor of the skin—of those parts unaffected by pigment deposits—and a weak, soft, extremely small pulse, indicate the failing circulation. The impulse of the heart grows weaker and weaker, and a soft blowing murmur is audible at the base and over the course of the great vessels. So exceedingly weak does the heart become, that the patient, when still able to sit up, may have no pulse at the wrist. The skin is cool and the temperature is below normal, although, under exceptional circumstances, an evening rise to febrile heat may be observed. Meanwhile, the gastro-intestinal disturbance increases ; the nausea becomes constant, vomiting occurs, and diarrhœa is added to the other causes of depression. Under these circumstances it may happen that death ensues before the occurrence of the characteristic pigmentation. No case, however, can be regarded as strictly typical in which the peculiar bronzing of the skin is entirely wanting. Those parts of the body exposed to the light first exhibit the change in color. The skin, in patches and streaks, and especially about old cicatrices, begins to grow dusky, or grayish brown ; then assumes an olive-green tint, and becomes, finally, bronze or copper-colored. As the tint deepens, it also widens, until the whole surface is dark—mulatto-like—those parts naturally pigmented staining most deeply, while the palms and soles, the nails, and the sclerotic remain white. The mucous membrane of the mouth, also, exhibits patches of pigmentation about the lips and cheeks, but especially along the margin of the teeth. Nothing could be more striking than such a change in the color of the integument, but not all cases present it in full, and an early termination may prevent anything like a general deposit of pigment. There may be in such cases only patches of pigment here and there, in situations where the coloring matter normally abounds, at the site of old cicatrices, and at points of pressure of clothing. Although cases undoubtedly exist in which all the symptoms of Addison's disease are present, save the pigmentation, they should not be regarded as examples of this affection, unless an early termination prevents the full development. It has been suggested that cases of this disease have indeed proved fatal before the peculiar pigmentation could develop, by a

persistent and uncontrollable vomiting, coupled with the usual asthenia. Sometimes diarrhœa has been associated with the gastric derangement, and the progress of the case accelerated by the gastro-enteritis, to which the fatal result was attributed. The simultaneous occurrence of so much pain and soreness in the epigastrium, of vomiting, and of extreme weakness, seems so much like the history of abdominal cancer, that a fatal result occurring before the pigmentation is attributed to cancer.

Course, Duration, and Termination.—The typical examples of Addison's disease are characterized by slowness of evolution. There are, however, cases much more acute in type, but these are decidedly in the minority. In these acute cases, after a period of unaccountable decline in health and activity, the patient goes to bed intensely prostrated, can hardly raise himself up, and on any muscular movements the members tremble. Nausea, vomiting, meteoric distention of the abdomen, and diarrhœa supervene, rapidly reducing the flesh and strength. The pulse grows quick and small, and the action of the heart, though rapid, is excessively weak. In these cases, usually, there is considerable febrile disturbance, quite in contrast to the subnormal temperature of the chronic type.

For many months in the ordinary cases the progress is very slow ; apparently, indeed, unchanged. Meanwhile the asthenia increases, the gastric disturbance grows worse, frequent vomiting occurs, and a severe, sometimes uncontrollable, watery diarrhœa sets in. Fainting on attempting to rise, severe *tinnitus aurium*, headache, failure of memory, great mental feebleness, muscular twitching, epileptoid seizures, are in turn experienced as the case progresses toward the end. Various abnormal nervous manifestations occur, and in one case (Broadbent's) choreic attacks came on. Meanwhile, the abnormal pigmentation increases until the whole body becomes intensely bronzed. The only termination is by death. In a large proportion the immediate cause of death is phthisis—tuberculosis frequently coexisting with the disease, if, indeed, Addison's disease is anything else than tuberculosis of the supra-renal bodies. The average duration of the cases is one and a half year. The most acute cases last about six months, while the most chronic extend over several years (Wilks). The duration is affected chiefly by the progress made in the general tuberculosis, or in the phthisis, associated with the majority of cases. Rossbach treats of the association of Addison's disease with scleroderma.* In many instances caries of the vertebra, psoas abscess, and inflammation and suppuration in the neighborhood of the capsules have existed.† The progress and termination may therefore be affected by these associated lesions. Those cases in which the usual coexistent diseases are wanting, and the anatomical changes are restricted to the supra-renal capsules, terminate by asthenia, and are the most protracted.

* Virchow's "Archiv," Band li, p. 100. † Greenhow, *supra*.

Diagnosis.—Until the characteristic discoloration of the skin appears, the diagnosis must be largely conjectural. A persistent and unaccountable asthenia, coinciding with an increase in the depth of color of the natural pigment, and the appearance of grayish-brown spots, ought to be rightly interpreted. Brownish spots appear on the face and other parts in some women during pregnancy and at each menstrual period, but in these cases the peculiar asthenia is absent. Greenhow describes * a case of "Vagabond's discoloration," which simulated Addison's disease; but the diagnosis was rendered easy by the free application of soap-and-water. Abnormal pigmentation occurs in some cases of exophthalmic goitre, but, while in this disease there is a marked degree of asthenia, the other symptoms of the morbid complexus readily determine its character. Anæmia should not be confounded with asthenia. The anæmia of chronic malarial poisoning, accompanied by more or less fawn-color of the skin, may be mistaken for the asthenia of Addison's disease. The distinction ought to be made between anæmia and asthenia, which will be confirmed by the previous history in both diseases. The discoloration of the skin when general may be confounded with jaundice, but the distinction is made by the extreme weakness which accompanies Addison's disease, and by the fact that in jaundice the change of color extends to the eye, to the mucous membrane, and to pathological fluids as well as to normal excretions, as the urine. Pityriasis versicolor is readily distinguished by the roughness of the skin, by the occurrence of the discoloration in patches, and by the presence of a parasitic organism. Furthermore, pityriasis versicolor does not materially affect the general health, and is not accompanied by the profound depression characteristic of Addison's disease. Leucoderma is readily diagnosticated by the accompanying patches of pigmentation and abnormal whiteness of the skin.

Treatment.—The treatment, although unpromising, is not without utility. There are two objects to be attained by remedies: to improve the cachexia; to relieve the more active symptoms. In the first group are such remedies as the sirup of the iodides of iron and manganese, cod-liver oil, chloride of calcium, quinia, iron, etc. Phosphorus has been given with obvious good results in several instances, and the phosphates and phosphites are excellent reconstituent tonics, which may be useful in this disease. Arsenic, also, is a promising remedy. Probably the best effects will be obtained from the administration of phosphorus in cod-liver oil, and the chloride of calcium with the sirup of the iodides.

For the nausea and vomiting, minute doses of Fowler's solution, bismuth and carbolic acid, and hydrocyanic acid, may be in turn tried. Tincture of nux vomica is an excellent stomachic tonic under these circumstances.

* "The Clinical Society's Transactions," vol. ix, p. 44.

MELANÆMIA.

Pathogeny.—The term *melanæmia* is applied to a condition of the blood in which are found small brownish or black masses, scarcely so large as a red-blood globule, of pigment matter. Sometimes these particles are oval, or round in shape, sometimes irregular, and rarely stratified by the presence of a colorless capsule (Rindfleisch). Occasionally true pigment-cells are observed. This pigment is found everywhere in the blood, but exists in greatest quantity in the spleen, which becomes, according to the quantity, a chocolate, brownish, or blackish color. The spleen may, indeed, be almost the sole place of deposit, but the liver is next in respect to place and quantity, and after the liver are the lungs, brain, and kidneys. Opinions differ as to the origin of the pigment, but the weight of authority is in favor of the splenic origin, and that it is a product of the disintegration of the red-blood corpuscles. As during malarial fever this destruction of the red corpuscles is more rapid than in any other form of acute infectious disease, melanæmia is a product of malarial diseases. The pathological changes characteristic of this state are found in the spleen, liver, lymphatic glands, marrow of bones, etc. The spleen is enlarged, its consistence soft, if there have been recent attacks, and firmer if considerable time has elapsed. The color depends on the quantity of pigment, and is dark slate, or brown, or black. The deposits of pigment take place chiefly along the veins, which are bordered by a dark line, and to a less extent along the arteries, and the whole splenic pulp may be tinted by it. The lymphatics and the marrow, also, contain pigment, which, with lymphoid cells, is found in the vicinity of the vessels. Characteristic changes, due to pigment deposition, also occur in the liver. As elsewhere, the pigment deposits are found alongside the vessels. According to Rindfleisch,* small extravasations of blood in Glisson's capsule, and in the parenchyma of the liver, initiate the pigment formation. The pigment granules accumulate about the branches of the portal vein and hepatic artery, about the intralobular and hepatic veins, but the hepatic cells are not involved. The whole organ has a steel-gray or blackish tint. Ultimately the nutrition of the organ may be so impaired that atrophy results.

As the pigment granules may be larger in caliber than the blood corpuscles, they will necessarily be arrested in those organs having a fine capillary network. Pigment embolisms of the cerebral vessels are, consequently, results of this process. Pigment blocking of the cerebral capillaries has precisely the same effects that other emboli produce: collateral hyperæmia, extravasations, and œdema, with the important structural alterations following in their wake.

* "Pathological Histology," American edition, p. 187.

Symptoms.—Melanæmia is an accident or complication of the severer cases of malarial fever. The changes in the spleen and liver do not cause symptoms, except the enlargement of the former organ, to be made out by palpation and percussion. The cerebral symptoms are, however, very pronounced. There are present, when the pigment embolisms occur, more or less intense headache, vertigo, delirium either low-muttering, or active and furious, passing into stupor, coma, and insensibility. There are occasionally paralysis and epileptiform attacks, but usually the motor disturbances are not more than twitchings of the muscles, ptosis and weakness of the muscles of the extremities. In cases seen by the author the delirium was wild—delirium ferox—and the motor troubles were those of paresis of muscular groups. In the author's cases also there was a very high temperature, to which the cerebral disturbance may have been in part due. In the more chronic cases, without fever, there are persistent headache and vertigo, the strength is easily exhausted, the nutrition inactive, and the surface, especially of those parts of the body exposed to the light, has a bronzed appearance. In such, we may assume that the pigmentation of the brain is confined to deposits alongside the vessels, and does not include embolic obstruction of the capillaries by pigment masses. When the last-mentioned condition exists, there will be more decided mental symptoms, epileptiform attacks, paralysis, etc. In the milder form, recovery may ultimately ensue if the patient be removed from miasmatic influences. In those cases of capillary embolisms, it is doubtful if recovery ever can take place. Nevertheless, treatment must be pursued from the symptomatic standpoint, for it may be that success will eventually be the reward of persistent efforts.

Treatment.—There are two therapeutical indications: to check the waste of red-blood globules; to effect the solution and extrusion of pigment. Quinine, iron, ergotin, and digitalis—which may be combined—are the most efficient remedies for the first indication; pyrophosphate of sodium for the second. If the symptoms are acute, quinia must be given in large doses—twenty to forty grains a day—if less so, five, even three grains three times a day. The other remedies should be prescribed accordingly.* The utility of the phosphate of sodium consists in its power to maintain the alkalinity of the blood, in its effects on the hepatic secretion, and in its influence over the metamorphosis of tissue.

HÆMOPHILIA.

Definition.—The term *hæmophilia* is applied to a congenital state characterized by the habitual occurrence of hæmorrhages. As the

* ℞. Quiniæ sulph. ʒ j, ferri redacti gr. x, ergotin ℈ j, digitalis gr. x. Make into ten wafers. One wafer three times a day. ℞. Sodii pyrophosphat. ʒ j, ferri pyrophosphat. ℈ j. M. Take a teaspoonful in sufficient water three times a day before meals.

disposition to bleeding is inherited, and is transmitted in families, persons so affected are called "bleeders."

Causes.—Heredity is the most important factor in its causation. It is an unfortunate fact that families of bleeders are remarkable for fertility. The males are affected thirteen times more frequently than females (Immermann*), but, on the other hand, women transmit the disease more certainly than males—for example, a male bleeder marrying a healthy woman, without taint of hæmophilia, has children usually free from this hereditary disposition; but a female bleeder marrying a healthy male has quite uniformly bleeder children. Again, if a woman, member of a bleeder family, but herself not a bleeder, marry, she will have some children who inherit the family taint. The disposition to bleeding usually manifests itself about the first dentition, and in a large proportion within the first year. The hæmorrhagic diathesis existing, a slight injury will suffice to start the bleeding: thus, lancing the gums, leech-bites, the Jewish rite of circumcision, slight cuts or abrasion of the skin, have been followed by uncontrollable hæmorrhage. The bleeding having once occurred, the tendency to attacks is thereby greatly increased.

Symptoms.—There does not seem to be anything peculiar in the bleeders as respects bodily conformation, temperament, habits, and disposition, except the hæmorrhagic diathesis, although it is said that they are usually persons of superior mental endowments (Legg†).

There are two distinct forms of hæmorrhage: the *external*, in which the blood pours out on the surface of the wound or abrasion; the *interstitial*, in which the blood diffuses into the interstices of the adjacent tissues. Frequently, if not usually, both forms occur at the same time. The external form may be the result of injury, and is therefore *traumatic*, or it occurs *spontaneously*, and is named accordingly. The external and traumatic form is single, for it is comparatively rare for more than one point of injury to exist at a time. On the other hand, the spontaneous hæmorrhage, indicating a more active state of the vice, may occur simultaneously at several points. The most usual site of the spontaneous hæmorrhage is the mucous membrane, especially of the oral and nasal cavity; of the stomach and intestines; of the bronchi; of the genito-urinary passages—named in the relative order of frequency. Recent cicatrices, that are still vascular, ulcers of the skin, and irritated surfaces, invite the hæmorrhage. Again, in the most perfect specimens of hæmophilia, bleeding occurs without any change in the skin to start it, and takes place from the fingers, toes, lobes of the ears, back of the hand, etc. By far the most common form of bleeding is

* Ziemssen's "Cyclopædia," vol. xvii, article "Hæmophilia."

† Dr. J. Wickham Legg, "Treatise on Hæmophilia," London, 1872, H. K. Lewis, p. 158.